THE ERYTHROCYTE SEDIMENTATION RATE

Choice of Technique for Sanatorium Use.

A Thesis for the Degree of M.D. Presented

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INTRODUCTION.

The object of the research reported in this thesis was to determine the best method of estimating the Erythrocyte Sedimentation Rate in a Sanatorium of 250 beds where the estimation is carried out monthly on every patient. Including staff and outpatients the number of estimations each week is about 70, so simplicity was desirable if it could be obtained without significant loss of accuracy.

In Part I the mechanism of the sedimentation reaction is discussed, and the factors influencing the reaction when it is studied in the test tube.

In Part II a selection of the methods which have been more or less widely used is reviewed in the light of the conclusions arrived at in Part I. Practical applicability to mass testing is also considered.

Part III is devoted to a group of case reports in which the clinical course is considered along with the Erythrocyte Sedimentation Rate estimated by the Westergren technique with the reading taken at the end of 2 hours.

HISTORY OF THE SEDIMENTATION REACTION

Fahreus (1921) gives an exhaustive survey of the history of the Sedimentation reaction, from which the following points stand out.

Phlebotomists from Hippocrates onwards noted that there was a difference between normal and pathological blood collected at a venisection; but a landmark appears when Hewson (1739-1744) noted that rapid sedimentation of the blood was the most important factor in the production of the buffy coat, which has always been considered a pathological phenomenon. Hewson and Nasse showed that accelerated sedimentation was not due to altered specific gravity of plasma or corpuscles. Then Nasse observed the tendency of the corpuscles to cluster in rapidly sedimenting blood. This agglutination of corpuscles in pathological blood was described by John Hunter in 1786. Gulliver noted that the rate of sedimentation was slow at first, then accelerated.

About this time, speculation on the cause of rapid sedimentation and formation of buffy coat was leading to the view that it depended on the quantity of fibrin in the blood. Biernacki, was the first to measure the sedimentation rate with a view to applying the test clinically; but unfortunately he worked on

the theory that the plasma was secreted by the corpuscles and he therefore measured the percentage volume of the supernatant plasma. He used a short wide tube, as this gave a larger plasma percentage in $\frac{1}{2}$ and 1 hour (because, until cell packing interfered with it, the rate of fall in a short wide tube would be the same as in a longer and narrower one).

MECHANISM OF THE SEDIMENTATION REACTION

Fahreus (1921) using citrated blood in test tubes of suitable length, observed that the rate of fall of the upper corpuscular layer accelerated at first until the packing of the cells as the botton of the tube caused deceleration. This suggested that the erythrocytes followed the hydrodynamic laws governing the fall of bodies in fluids. Stoke's law refers to spheres falling in fluid of infinite extent, but the basic principle of it holds good for bodies which are not spheres falling in confined space.

The essential formula is:-

$$V = \frac{2}{9} \cdot g \cdot \frac{s - s'}{\mu} \cdot r^2$$

Where V = maximum velocity of fall

g = 32 ft. per second

s = specific gravity of falling body

s' = specific gravity of fluid

μ = viscosity of fluid

r = radius of falling body.

Fahreus therefore postulated that increased E.S.R. must be due to one of five causes.

1. Increased S.G. of erythrocytes.
2. Decreased S.G. of plasma
3. Decreased viscosity of plasma
4. Increased size of erythrocytes
5. Agglutination of erythrocytes

1 and 2 were ruled out experimentally by Fahreus.

3. The viscosity of plasma is greater in the more rapidly sedimenting bloods, owing to increase in plasma proteins. Tang and Wang (1941) consider that increased plasma viscosity is a better index of disease activity than the E.S.R. Also a study of the formula above suggests that where the difference in S.G. between the body and the fluid is small, as it is with erythrocytes and plasma, viscosity is a minor factor in determining the velocity. Fahreus demonstrated the truth of this by dilution experiments. The recent work on this by Whittington and Millar is referred to later.

4. Increase in the size of single erythrocytes could only very slightly increase the rate of sedimentation. Unagglutinated corpuscles suspended in isotonic citrate or saline solution sediment very slowly (about 0.5 mms. per hour) so even doubling the size of the erythrocytes would not produce a pathological E.S.R.

5, In normal citrated or oxalated blood the erythrocytes form rouleaux by joining flat surface to flat surface; but the rouleaux are made up of a few erythrocytes only. In rapidly sedimenting blood the rouleaux are long, and are joined together to form clusters which are visible to the naked eye in the sedimentation tube, as in Hunter's observation on venisection blood. I have counted rouleaux of 12

erythrocytes in normal blood, but in rapidly sedimenting bloods the erythrocytes in the clumps are uncountable. Fahreus made an approximate calculation by Stoke's formula that there were over 100,000 erythrocytes in the clumps in one pathological blood. This agglutination of erythrocytes is therefore the only factor which could cause the E.S.R. to increase to the extent seen in many diseases.

The increased agglutination of erythrocytes in rapidly sedimenting bloods is associated with an increase of fibrinogen and/or serum globulin in the plasma (Fahreus 1921, Westergren 1924) and the increase in these is associated with an increase in the viscosity of the plasma (Tang and Wang 1941, V.S.) The latest work on this question (Whittington and Millar 1942) is an abstruse mathematical study on the viscosity of blood and plasma related to the maximum velocity of sedimentation in controlled conditions, but it does not bring appreciably nearer the time whenviscometry will replace estimation of the E.S.R. in the ordinary laboratory.

In order to discover whether or not the sedimentation producing properties of the plasma are exhausted or reduced by causing Sedimentation once, the following experiment was carried out.

EXPERIMENT I

Blood 8 cc. diluted with 3.8% citrate solution 2.c.c. was divided between two centrifuge

tubes. From tube 1 (6 c.c.) a Westergren sedimentation specimen was set up immediately and the remaining 5 c.c. left to sediment in the centrifuge tube. Tube 2 was centrifuged for 20 minutes, then the plasma was pipetted off and measured, and the cells washed. This specimen was then reconstituted with a quantity of plasma from tube 1 equal to the quantity removed before washing the cells. This tube 1 plasma was obtained by gentle centrifuging after sedimentation had been allowed to proceed for 40 minutes i.e. until it was approaching its maximum velocity of sedimentation. A Westergren sedimentation specimen was then set up from the reconstituted tube 2. The results are shown in the table.

TUBE 1.	TUBE 2.
1st Hour 8 mm.	5 mm.
2nd " 22.5 mm.	14.5 mm.
M.V. 25mm/100 min.	20 mm/100 min.

This shows that there was a slowing of the E.S.R. in this case when "used" plasma was mixed with washed cells - a slowing probably beyond the experimental error of reconstituted blood experiments. The results must therefore be considered suggestive but not conclusive.

FACTORS INFLUENCING THE E.S.R.

In order to assess the value of various methods of estimating the E.S.R. it has been necessary to study separately the factors that influence sedimentation rate when the sedimentation reaction takes place in the limiting conditions of a laboratory test tube, The conclusions arrived at in the following pages are biased in favour of technical simplicity, and the term Maximum Velocity of Sedimentation indicates the maximum velocity attainable in the normal type of tube in which cell packing has some slight effect from the very beginning of the test. Higher velocities are attainable in bulb bottomed tubes in which the bulb will accommodate the packed cells. The increase in velocity in such tubes may be up to 10%

THE EFFECT OF TEMPERATURE ON THE E.S.R.

The fact that the E.S.R. is slowed by reduction of temperature of the test has long been recognised. Most workers, however, appear to agree with Plass and Rourke (1929) that, within the limits of normal laboratory temperatures, the effect is hardly significant.

It was observed at the Cheshire Joint Sanatorium a number of years ago that the range of E.S.R. in the patients was significantly more rapid in summer than in winter. This led to the installation of a constant temperature cabinet controlled thermostatically at 65°F. That temperature was chosen because it is easier to heat the cabinet in winter than to cool it in summer. In a warmer climate it would be advisable to control the temperature at a higher level. The cabinet is heated by two carbon filament bulbs with asbestos shields in front of them to protect the sedimentation tubes from direct radiation. The front is of glass so that readings may be taken without disturbing the temperature.

For all my own work I have used this constant temperature cabinet. The necessity for this was confirmed by a number of observations on duplicate

specimens set up from the same blood samples, one in the constant temperature chamber and the other on the laboratory bench in normal winter weather. (Experiment 2.).

Table 1 gives the results, 2nd hour reading on a Westergren 200 mm. tubes, which show that marked slowing of the E.S.R. may result from a temperature drop of only 9°F, and also that the response of the E.S.R. to fall in temperature is so erratic that a correction factor could not be found. Even blood samples from the same donor behaved differently on different days although technique was rigidly standardised.

Day (1940) attributes E.S.R. variation with temperature to slower agglutination of the erythrocytes when the temperature is lower, with the consequence that the maximum velocity of sedimentation is reached later, He held, however, that the maximum velocity, though reached later, is the same in the warm as in the cool specimen. This is not in keeping with my findings in experiments where the difference in temperature between the specimens was sometimes as little as 7°F. The variations in M.V. (Table 2) are as striking as the variations in 2nd hour reading, and as erratic. Two specimen sedimentation charts are appended (Nos. 1 and 2.).

Table 1. Westergren 2nd Hour Reading at Various Temperatures

65 F.	58°	57°	56°	55°	53°	52°	50°	49°
9								5
10	7.5							
14		14		14				
15						11.5		
16				14			6	
18			10				5	
26	20			20				
36		34						
40							34	23
44			34				32	
49						38		
59.5					37.5			
61					51			
66								54
80						77		

TABLE 2. M.V. in mm/100 min. at Various Temperatures.

65 F.	58°	53°	52°	49°
10				4.5
10.5	8			
20			15.5	
26.5	25			
46				32
52			44	
55		47.5		
73.5		38.5		
85				75
92			116	

CHART 1.

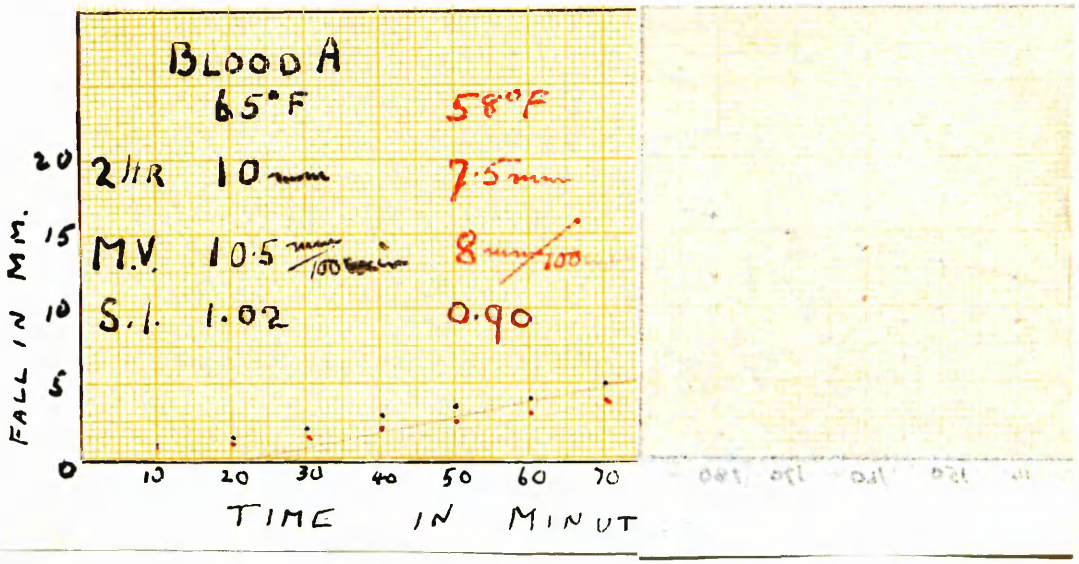
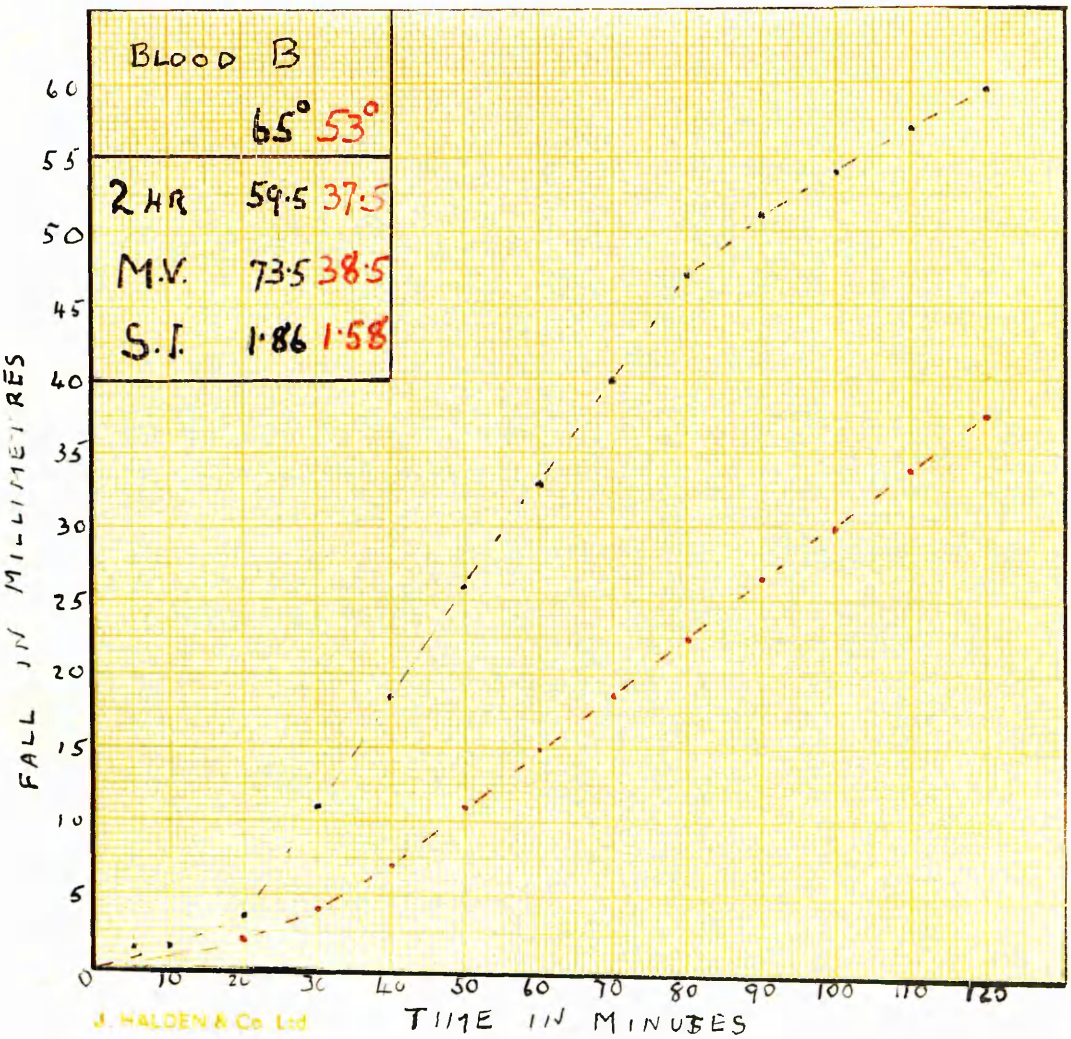


CHART 2.



THE EFFECT OF THE CELL VOLUME OR CELL COUNT ON THE E.S.R.

So much work has been done on this question, that apart from two experiments demonstrating that the findings of others are confirmed when the Westergren 200 mm. tube is used I will confine myself to a review of the literature.

EXPERIMENT 3.

Object: To determine the affect of anaemia on sedimenting blood by varying the proportion of cells to plasma, maintaining the proportion of anticoagulent approximately constant.

Blood 9.5 cc. diluted with 3.8% citrate solution 0.5 cc. was centrifuged and the plasma removed. The cells were washed with citrate solution and the washed cells suspended in an equal volume of the citrated plasma. From this suspension four specimens were prepared, as shown in the table, by mixing varying quantities of cell suspension and plasma with a uniform quantity of citrate solution. It is estimated that the slight increase in citrate content as the dilution of cells increases will be compensated by the lesser quantity of citrate carried by the lesser volume of washed cells.

TABLE I

	Cell Suspension	Citrated Plasma	3.8% Citrate Sol.	Total
1.	1.2	-	0.2	1.4 cc.
2.	1.0	0.2	0.2	1.4 cc.
3.	0.8	0.4	0.2	1.4 cc.
5.	0.6	0.6	0.2	1.4 cc.

The four dilutions were set up in Westergren 200 m.m. tubes in the constant temperature cabinet and the resulting sedimentation observed for 3 hours at 10 minute intervals. The experiment was repeated using a moderately rapid sedimenting blood. The results are tabulated below.

TABLE 4.

Blood	Dilution	2nd Hour	M.V.	Log M.V.
A	1	4	4.5	0.65
	2	16.5	17.5	1.24
	3	36.5	35	1.54
	4	74.0	73.5	1.87
B	1	24	26	1.41
	2	58	60	1.78
	3	88	88	1.94
	4	120	138	2.14

This confirms that reduction of cell volume is associated with increase in E.S.R.

EXPERIMENT 4.

An in vivo experiment was attempted. An E.S.R. estimation and erythrocyte count were carried out on a blood donor immediately before bleeding. Two days later these tests were repeated.

Result: TABLE 5.

	Before Bleeding	After Bleeding.
R.B.C.	4,675,000	4,045,000
E.S.R.	15 mm/2 Hr.	15 mm/2 Hr.

A plasma analysis would have added considerably to the value of this experiment.

It is obviously necessary to employ some method of correcting the E.S.R. to standard cell count or cell volume if conclusions are to be drawn from a single test. But a case can be made for omitting this correction in serial tests.

a. In the great majority of patients the blood count does not vary greatly during the period of observation. Therefore the comparison of serial results is reasonably accurate. Exception must be made for cases of copious haemoptysis and for cases undergoing major surgical intervention with considerable blood loss, such as thoracoplasty.

b. The obviously anaemic patient is treated for anaemia until the blood count returns to normal. Improvement in the E.S.R. during the period of treatment for anaemia may be discounted when results are assessed. Thereafter comparable results will be obtained.

c. Any method of correction to normal blood count entails the expenditure of a considerable amount of time by a skilled worker. It would multiply the man/minutes required for the test, if the simple method advocated later is employed, by not less than three. This would greatly reduce the number of tests that could be carried out at the same time, and in most institutions the test could not be carried out so frequently as is clinically desirable.

d. The best correction methods require more blood than the simple test. This means that correction could not always be carried out, as the required quantity of blood may not be obtained from patients in poor condition.

METHODS OF CORRECTING THE E.S.R. TO A NORMAL CELL COUNT OR CELL VOLUME

a. The blood sample may be adjusted by withdrawal or addition of plasma to bring the erythrocyte count to a standard figure, say 5 million. This is the method advocated by Schuster (1938) and Walton (1933). The blood count is adjusted according to the formula of Blacklock (1921). This method has the great advantage that it is universal and not applicable to only one method of estimating the E.S.R. Also, Schuster formed the impression from a considerable volume of experimental work, that other methods of correction were not reliable. The time required for the correction is considerable as it entails an erythrocyte count. In all but severely anaemic cases (R.B.C. 2 million) 4 cc. of blood is sufficient for making up a corrected sample when using the Westergren Technique.

b. The numerical correction method advocated by Collins et al (1939) is applicable only to their own method of estimating the E.S.R. which is considered in detail elsewhere. The sedimentation is observed in unadjusted blood and the result corrected to correspond with the same blood adjusted to a packed cell volume of 42% by the addition or subtraction of a factor which they arrived at experimentally.

c. The graphical correction table devised by Rourke and Ernstene (1930) takes into account the fact that the more rapidly sedimenting bloods are more affected by reduced cell volume then slow sedimenting bloods. It also is only applicable to their own method of estimating the E.S.R. which is the laborious one of determining the maximum velocity of sedimentation. The packed cell volume (P.C.V.) is determined and the M.V. corrected to correspond with a P.C.V. of 45%. According to the authors six to eight tests fully occupy an observer for 1½ to 2 hours. Therefore to carry out the 70 tests a week which are carried out at the Cheshire Joint Sanatorium would occupy a trained laboratory worker for at least 15 hours - two full working days.

d. The correction graph employed by Gram (1929) for the Westergren technique is based on the haemoglobin percentage instead of the erythrocyte count or packed cell volume. This makes it simpler to carry out, but obviously less accurate.

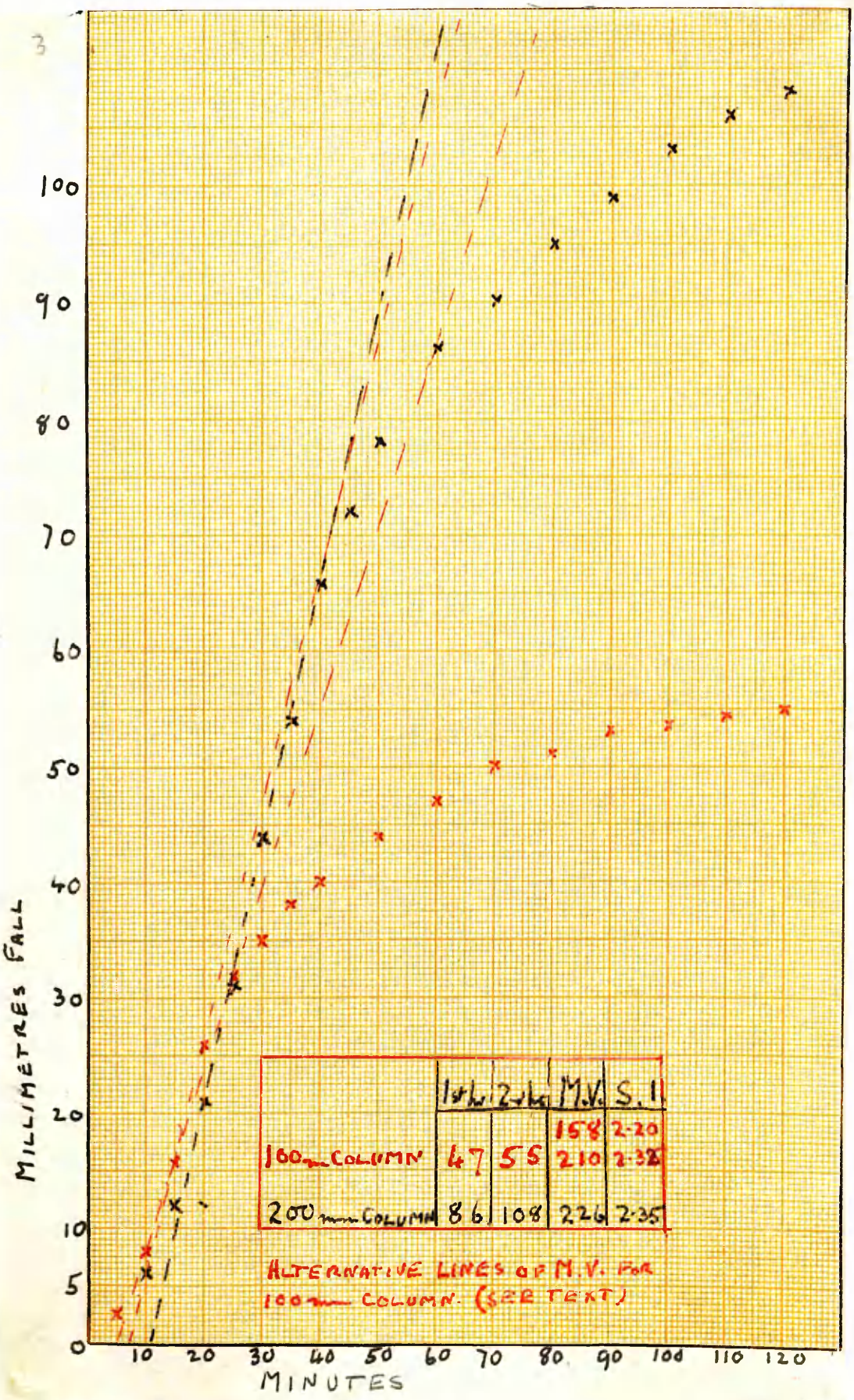
e. The method devised by Rees & Walton (1933) is simple and ingenious but is applicable only to his technique.

Schuster's work indicates that correction of the sample to a standard erythrocyte count or cell volume is more accurate than any graphical or arithmetic method.

THE HEIGHT OF THE COLUMN OF BLOOD

It has been noted above that the sedimentation of erythrocytes in a suitable test tube may be divided into three periods, acceleration, maximum velocity, and deceleration due to packing. As the phenomenon we wish to measure is the velocity of sedimentation, any method which does not permit the blood to reach its maximum velocity is bound to reduce the sensitivity of the test for the more rapidly sedimenting bloods. Schuster (1938) tested the effect of columns 200 mm, 100mm, 50 mm and 35 mm. high, and decided to use the 100 mm. column, apparently because it was easier to obtain the necessary quantity of blood. Day (1940) plotted the sedimentation of four blood samples in columns 200 mm, 100 mm and 60 mm high, and showed that the most rapidly sedimenting of his four blood failed to reach its maximum velocity of sedimentation in the 60 mm and 100 mm columns, because packing had begun to take effect before the maximum velocity was reached; while only the slowest sedimenting sample reached its maximum velocity in the 60 mm column. On the attached chart (Chart 3) I have plotted the sedimentation of a rapidly sedimenting blood in 200 mm. and 100 mm. columns at 5 minute intervals for the first hour and thereafter at 10 minute intervals. (Experiment 5.). It will be seen that the 100 mm. column almost succeeded

CHART 3.


MILLIMETRES FALL
0
5
10
20
30
40
50
60
70
80
90
100
10
20
30
40
50
60
70
80
90
100
110
120
MINUTES
1st W. 2nd W. M.V. S.I.
100 mm COLUMN 47 55 158 2·20
210 2·38
200 mm COLUMN 86 108 226 2·35
ALTERNATIVE LINES OF M.V. FOR 100 mm COLUMN. (SEE TEXT)

in reaching its maximum velocity for five minutes only. But the possible error involved in drawing a line of maximum velocity through two points only is large. In normal tests at least three points are always included. If this is done on Chart 3. the M.V. for 200 mm and 100 mm columns becomes not 240mm/100 min. and 210mm/100 min. but 240 and 156. The lack of sensitivity of both the 1st and 2nd hour reading in the 100 mm column for such rapidly sedimenting bloods is obvious when it is borne in mind that moderately rapid sedimenting bloods would show approximately equal readings at 1 hour in 100 mm. and 200 mm. columns, and slow sedimenting bloods would be equal at both 1 hour and 2 hours.

Though this reduction of sensitivity at the higher sedimentation rates is not of great clinical significance, I favour the 200 mm. column, which was Westergren's (1921) choice, as I do not find that Schuster's argument regarding the difficulty of obtaining the necessary blood holds good. In an experience of some thousand of tests on tuberculous men and women I have found that when one succeeds in obtaining blood, the quantity is sufficient for the 200 mm. column. The exceptions have been roughly 1 in 1000. Less than 2% of female patients occasionally miss a monthly test through failure to obtain blood at all.

BORE OF TUBE

It has been observed that the bore of the tube used for the test may have some effect on the E.S.R. Ham & Curtis (1938) who used oxalated blood for their tests, found that there was slowing of the E.S.R. and irregularity of results when the tube bore was less than 2 mm. and that there was some slowing when the bore was 2.5 mm. (the Westergren pipette). The effect was investigated using citrated blood (20% of 3.8% sodium citrate solution) in pipettes giving a height of column of 200 mm. with the following bores:- 1.1 mm, 1.2 mm, 1.3 mm, 2.0 mm, 2.6 mm (this was a Westergren pipette) 3.6 mm and 4.2 mm. The tubes were calibrated by me by the mercury method.

EXPERIMENT 6.

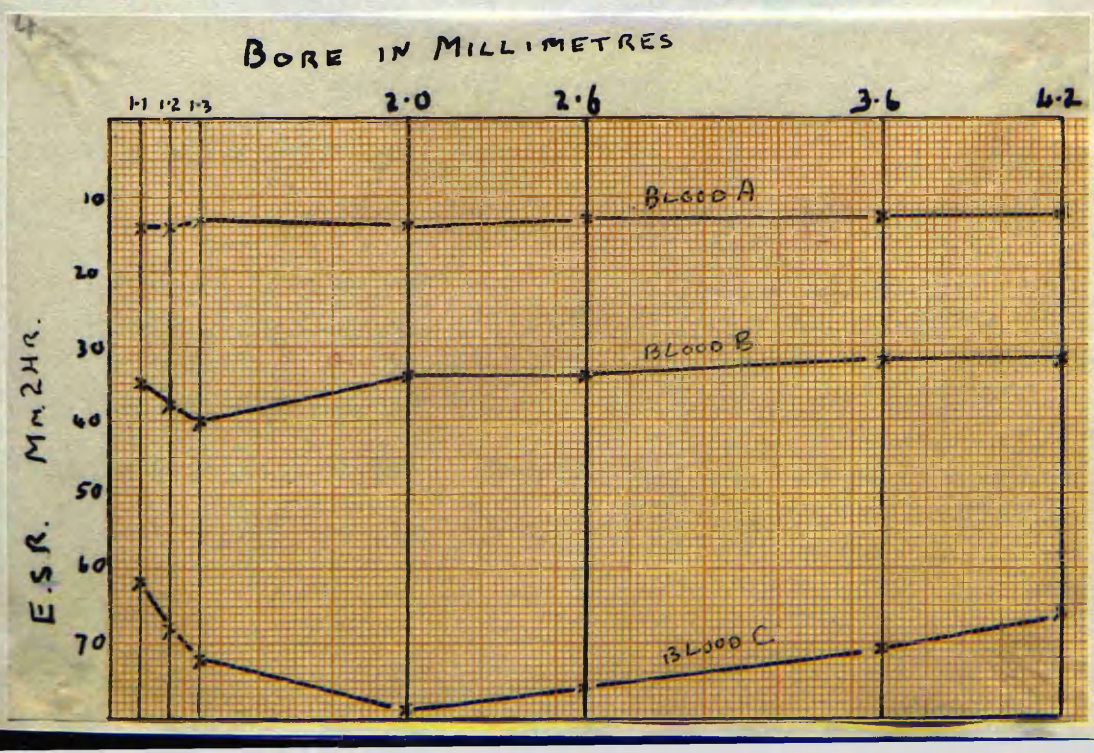
Parallel tests each from a single blood sample, were carried out on slow, moderate, and rapidly sedimenting bloods. The results are shown on the graph.

It appears that tube bore down to 1.1 mm. has little effect on slow sedimenting blood. With moderately rapidly sedimenting blood the bore of the tube has no significant effect until the bore is reduced below 2 mm. Below that there is significant irregularity. With rapidly sedimenting blood the bore of the tube has more effect. The most rapid

E.S.R. was obtained in the 2.0 mm tube. Below this bore there was significant slowing and there was also slowing in the wider tubes, though not so marked.

Variation above and below the reputed bore of standard tubes probably does not exceed ± 0.1 mm. Such variations will not cause significant variations in the E.S.R. until the smallest tube bores are reached. Observation of sedimentation taking place in narrow tubes (1.0 mm - 1.5 mm) suggests that irregularities of sedimentation occur when the rouleaux-aggregates are of such size in comparison with the bore of the tube that they can no longer fall free in the plasma. The displaced plasma appears to flow up in the periphery of the tube while the falling rouleaux aggregates form a solid looking core. In such circumstances it is not surprising that irregularities in E.S.R. are found.

CHART 4.



CHOICE OF ANTICOAGULENT

The following anticoagulents have been recommended by various authors.

1. Sodium Citrate, dry or in solution of strength varying from 2% to 5%
2. Oxalates, either dry or in solution
3. Heparin or Hirudin
4. Chlorazol Fast Pink.

Ham & Curtis (1938) make a good theoretical case for a dry oxalate mixture containing ammonium and potassium oxalate, as recommended by Heller and Paul (1934). This has the minimum effect on the erythrocytes, and the blood is not diluted.

My own experience makes me favour 20% of an isotonic (3.8%) solution of sodium citrate for the following reasons:-

1. The danger of clotting in the syringe when taking the specimen is eliminated.

2. Oxalated blood sometimes behaves erratically in tubes of 2.5 mm. bore.

3. Variations in E.S.R. due to slight error in the quantity of blood or citrate solution is less when 20% of the citrate solution is used than when 10% is used as recommended by Walton (1933).

4. The anticoagulent should be isotonic with blood (e.g. 3,8% sodium citrate) so that it will have the minimum effect on erythrocytes.

5. 20% of citrate solution is the most universally used anticoagulent in Europe. Any other would have to show definite advantages before a change could be advocated.

DAY TO DAY VARIATIONS IN THE E.S.R.

In a recent paper Greene (1941) reported a series of observations on normal women in which he failed to find any correlation between variations in the E.S.R. (Westergren 1st hour) and the menstrual period. However, all his cases did show a variation in the E.S.R. from day to day, considerable in some. Greene does not say that temperature was controlled during his observations, so it was decided to do a small series of daily observations on the E.S.R. of two quiescent working tuberculous subjects. (Experiment 7). The temperature of the test was controlled at 65°F. Westergren 200 mm. tube, 1st and 2nd hour reading.

The results are shown in Charts 5 & 6. The fact that Subject A. developed Coryza on the third day possibly adds to the interest of the experiment. The fact that Subject B felt well throughout although his E.S.R. showed a rise corresponding with that of A, with whom he shares a laboratory for some hours a day is of interest. It seems reasonable to assume that a sub-clinical infection was responsible for the rise.

Cutler (1929) suggests that the small variations in normal subjects are due to increase or decrease of activity, as there is more tissue break-down in the active subject.

My series of results is far too small to warrant any conclusions, but one cannot obtain 2 cc's of blood daily at the same hour from the same subject indefinitely. However, taken in conjunction with Greene's series, one is forced to conclude that minor variations in the E.S.R. may have no clinical significance in relation to Pulmonary Tuberculosis.

CHART 5.

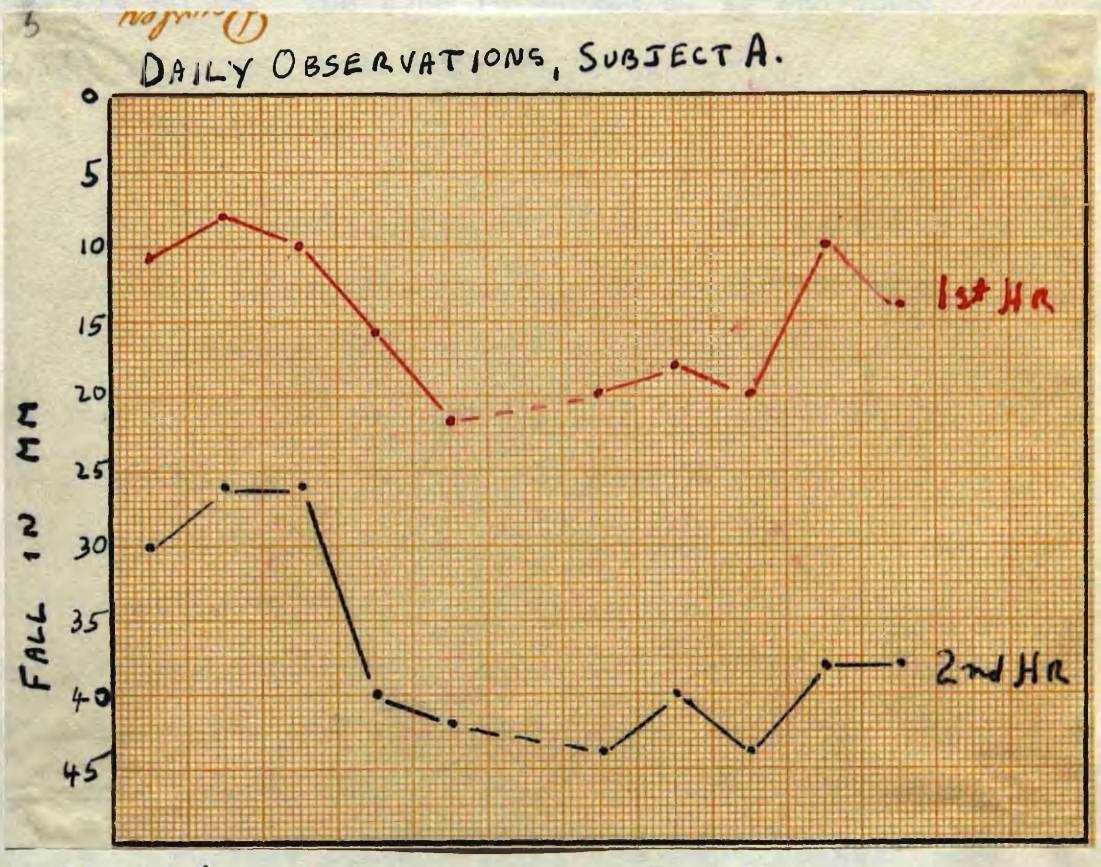
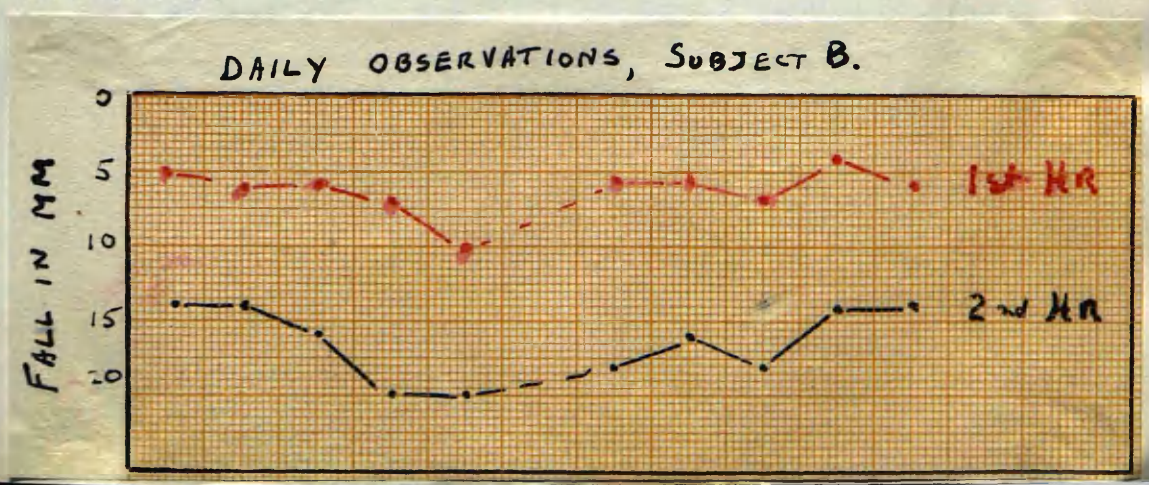


CHART 6.



THE LINZENMEIR METHOD.

Linzenmeir (1920) uses a round bottomed tube with a bore of 5 mm. marked at a volume of 1 cc. This gives a height of column of approximately 50 mm. The tube is marked 6, 12 and 18mm. below the 1 cc. mark. The anticoagulent is 20% of a 5% solution of sodium citrate.

The result measured is the time the upper corpuscular layer takes to fall to the 18 mm. mark.

Although this method is fairly widely used in America it has the great practical disadvantage that instead of an alarm clock giving warning at fixed times for readings the observer must watch the test continuously in the early stages with rapidly sedimenting bloods, and as the low limit of normality is 5 hours the test may not be completed until this time has passed.

Further disadvantages are the shortness of the column, and the anticoagulent which is not isotonic with blood.

MICRO METHOD (LYLE CUMMINS & ACLAND)

The tube has a bore of about 1.5 mm. and a length of $4\frac{1}{2}$ inches. One end is drawn out into a capillary stem. At the other end it is marked at a volume of 0.02 cc. and 0.08 cc. Using a rubber teat and adaptor fitted to the capillary end, 0.02cc. citrate solution (3.8%) and 0.08 cc. blood from a finger prick are measured and mixed in a watch glass. 0.08 cc. of the mixture is drawn up into a similar pipette and then drawn up beyond the mark. The capillary end is then sealed in a flame and the tube set up in a rack. The fall of the upper corpuscular layer is measured in millimetres at 5 hours and 24 hours, and expressed as a percentage of the column.

This method might be of use in children and in adults in whome no veins can be found, for it uses less blood than any other suggested method. But it does not approach the standard of accuracy desirable in a routine method for the following reasons.

1. Variations in tube bore may cause considerable change in E.S.R. in tubes about 1.5 mm. bore.

2. The height of the column is less than 50 millimetres, so many bloods would not reach their maximum velocity of sedimentation before packing caused deceleration.

3. The technique of setting up is not easy.

WALTON'S METHOD

Walton (1933) used 4.5 cc. of blood and 0.5 cc. of 3.8% citrate solution. The specimen on which the test is carried out is corrected by Blacklock's method to a cell count of 5 million per c.mm. The tube bore is 6 mm. and the height of column 32.5 mm. The fall of the upper corpuscular layer is measured at 1 hour.

Instead of correcting the cell count of the specimen, a simple and ingenious graphical method of correction may be used if the blood count is over 3 million.

The height of column is so short that only slow sedimenting bloods have a chance of reaching their maximum velocity of sedimentation, and it is probable that they will not have reached it by the end of 1 hour. The maximum possible fall is roughly 17 millimetres, so the range of results is very limited. Finally, test tubes of this bore are much more difficult to clean than pipettes, and absolute cleanliness is necessary to obtain accurate results.

WINTROBE'S METHOD.

Wintrobe's method aims at obtaining the maximum amount of information from a single specimen of blood. Oxalated blood is used. The tube is 11 cm. long, parallel sided and flat bottomed, bore about 2.5 mm. It is graduated in millimetres to 10 cm. from the bottom, and is filled by means of a long fine pipette to the 10 cm. mark. After the E.S.R. has been obtained by whatever method the observer favours, the tube is centrifuged at 3,000 r.p.m. for 30 minutes. The packed cell volume, (P.C.V.) thus obtained can be used for correcting the E.S.R. to a normal P.C.V. by the method of Rourke and Ernstene (1930).

Other observations suggested by Wintrobe are:-

1. Information regarding anaemia or polycythaemia is obtained from the P.C.V.

2. Information regarding Leucocytes and Platelets may be obtained from the intermediate layer between the R.B.C. and the plasma.

3. The Icterus Index may be determined on the supernatant plasma.

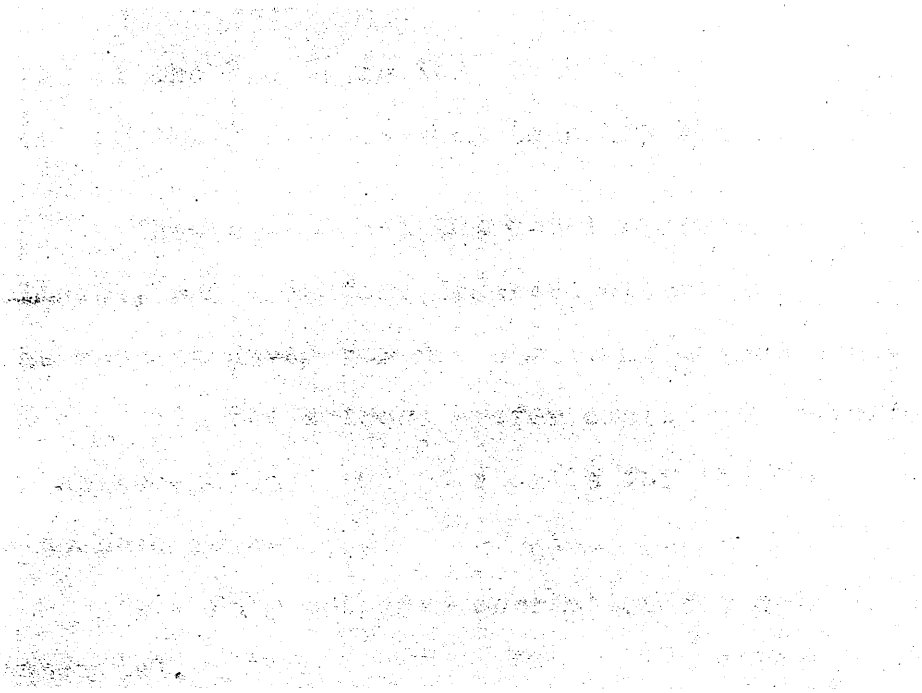
The test may therefore be of value to the clinical pathologist, though it would serve only as an indication for further investigations. For simple estimation of the E.S.R. it possesses some disadvantages.

1. The 100 mm. column does not permit rapidly sedimenting bloods to achieve their maximum velocity of sedimentation.

2. Oxalated blood does not always behave as it should in a tube with 2.5 mm. bore (Schuster 1938).

3. The tubes are difficult to wash, and absolute cleanliness of glassware is essential for reliable results.

4. Correction scales for anaemia are not considered reliable (Schuster 1938).



THE WIDE BORE TUBE METHOD used at four Rheumatic Clinics (Colins, Gibson, Race & Salt, 1939).

For this method a 5 cc. conical tube (centrifuge type) is used, graduated in 100 parts by volume. The height of the column of blood is approximately 72 mms. and the diameter of the upper (parallel) part is 12 mms. Oxalated blood is used, and the volume of cells at the end of 1 hour is reported, as suspension stability (S.S.) after Fahreus, rather than sedimentation rate. The packed cell volume is estimated in a haemocrit tube, and the observed S.S. corrected to a standard cell volume. of 42% by the application of a factor.

(a) If the P.C.V. is less than 42% add 1.5 (42 - P.C.V.)
(b) If the P.C.V. is more than 42% subtract 1 (P.C.V.- 42)

This method has the backing of four important clinics, and therefore deserves attention.
The reasons given for the choice of method are:-

1. The authors prefer oxalate to citrate as an anticoagulent, and this calls for the use of a wide bore tube.

2. They consider correction for cell volume essential.

3. They are satisfied with a clinical application of the test.

There are, however, considerable theoretical and practical objections to the method.

1. Volume is reported instead of distance, though the velocity of sedimentation of the erythrocytes has no connection with the volume of the sample. This would not matter if the tube was a cylinder because then volume and distance would be directly proportional to one another.
2. The height of the column is too short for any but fairly slow sedimenting bloods to reach their maximum velocity of sedimentation (see under "Height of Column").
3. With the short column and tapered tube employed, packing becomes an important factor and the effects of altered cell volume are therefore exaggerated; and the correction for cell volume is therefore essential.
4. The volume of blood required is more than can be obtained with any certainty from ill female patients, and when oxalate is used as anticoagulent the blood must be drawn rapidly, or clotting commences in the syringe.
5. The time spent on each test is at least 10 minutes, which compares unfavourably with the 3 minutes or less spent on each blood when using the Westergren technique without correction for anaemia.

THE CUTLER 1 cc METHOD.

Cutler has described a 5 cc. method, a 1 cc. method and a finger prick method, but he prefers his 1 cc. method (Cutler 1929).

Citrated blood (10% of a 3% solution of sodium citrate) is used in a tube with 5 mm. bore. The column height is 50 mm. The fall of the upper corpuscular layer is plotted on a graph at 5 minute intervals for 1 hour.

From this graph is determined:-

1. The type of curve. Four types of curve are described.

2. The fall in 1 hour. This is important for the two slower sedimentation types of curve.

3. The time at which packing slows sedimentation to less than 1 mm/5 minutes. This is important for the two rapidly sedimenting types of curve.

This is an ingenious attempt to overcome the inherent disadvantages of a short time and short column technique. But if a multiple reading method is to be used there are sound theoretical reasons for determining the maximum velocity of sedimentation. This calls for a longer column of blood, but if the tube bore is decreased the quantity of blood required will remain small.

As in all narrow bore tube, as opposed to

pipette methods, it is difficult to clean the tubes.

No reason is given for not using an isotonic solution of anticoagulent.

THE SEDIMENTIN INDEX.

Day (1940) claimed that the figures used in his method of expressing the E.S.R. have an absolute value, i.e. 1 unit always represents the same quantity of sedimentation producing substances in the blood. This is the first time such a claim has been made, and if it could be substantiated it seems that the Sedimentin Index would be the method of choice.

The Sedimentin Index (S.I.) is the log of the maximum velocity of sedimentation (expressed in millimetres per 100 minutes) determined in a Westergren 200 millimetre tube. It is based on a series of experiments which have been examined and repeated by me where necessary.

Day's Experiment VI demonstrates that in the absence of plasma, erythrocytes suspended in citrate solution do not agglutinate, and the slightly different rates of sedimentation of different percentage suspension are presumably the result of the different viscosities of the different suspensions.

In Experiment VII he claims to demonstrate that equal volumes of plasma added to various percentage suspensions of erythrocytes in citrate solution caused identical maximum velocity of

sedimentation in all suspensions. If this result could be confirmed one could conclude that:-

1. Citrate solution has no effect on the sedimentation rate.

2. The viscosity of the specimen has no effect on the sedimentation rate.

3. The plasma alone determines the sedimentation rate.

Day accepts these findings in his later experiments, though recent work by Whittington & Miller (1942) confirms that the second is a falacy.

This experiment was repeated by me using bloods of varying sedimentation rates.

EXPERIMENT 8.

Object: To determine the effect of a constant proportion of plasma on the sedimentation rate of a reconstituted blood with varying proportions of cells and citrate solution.

METHOD. Blood 9 cc. diluted with 3.8% citrate solution 1 cc. was centrifuged and the plasma removed. The cells were washed, and the washed cells suspended in citrate solution (80% cells 20% sol.) From this suspension five specimens were prepared, as shown in Table 6, by mixing varying quantities of cell suspensions and citrate solution with a uniform quantity of citrated plasma. Only 10% of anti-coagulent was used so that the concentration of

anticoagulent in the separated plasma would be approximately 20%.

TABLE 6.

	Cell Suspension		Citrated Plasma		Citrate	Total
	Cells	Citrate	Plasma	Citrate		
1.	0.56	0.14	0.64	0.16		1.5 cc.
2.	0.48	0.12	0.64	0.16	0.10	1.5 cc.
3.	0.40	0.10	0.64	0.16	0.20	1.5 cc.
4.	0.32	0.08	0.64	0.16	0.30	1.5 cc.
5.	0.24	0.06	0.64	0.16	0.40	1.5 cc.

The five dilutions were set up in Westergren 200 mm. tubes in the constant temperature cabinet and the sedimentation observed at 10 minute intervals for 3 hours.

The experiment was repeated using bloods of different sedimentation rate. The results are tabulated below.

TABLE 7

	Dilution	2nd Hour	M.V.	Log M.V.
Blood A	1.	20	21.5	1.33
	2.	19	22	1.34
	3.	25.5	28.5	1.45
	4.	28	31.5	1.49
	5.	33	35	1.54
Blood B	1.	40	42	1.62
	2.	40	44	1.64
	3.	42	41	1.61
	4.	51.5	51	1.70
	5.	43	42	1.62.
Blood C	1.	83	100	2.00
	2.	88	103	2.01
	3.	105	117	2.07
	4.	124	140	2.15
	5.	137	156	2.19

Table 7 (Cont'd)

	Dilution	2nd Hour	M.V.	Log M.V.
Blood D.	1.	clotted		
	2.	90	109	2.04
	3.	95	112	2.05
	4.	101	130	2.11
	5.	112	135	2.13
Blood E.	1.	54.5	56.5	1.75
	2.	60	58.5	1.77
	3.	66	63	1.80
	4.	71	66.5	1.82
	5.	79.5	74	1.87

CONCLUSIONS

Day's results are not confirmed. The trend of all samples except Blood B was to sediment more rapidly as the cell percentage diminished and citrate percentage increased. Though other factors probably come into play, some working in the opposite direction, the obvious key factor is viscosity. If the basic principles of Stoke's Law have anything to do with the erythrocyte sedimentation rate, it is obvious that the E.S.R. must be increased when the viscosity of the fluid in which the erythrocyte clumps are falling is reduced, as it is in this experiment, by the addition of increasing quantities of citrate solution.

A possible explanation of Day's anomalous result is that he was using exceedingly weak cell suspensions varying from 30% cell volume down to 6.6% In the weaker dilutions the erythrocytes are obviously far apart. The same total amount of agglutinating substances may fail in these circumstances

to form erythrocyte clumps of the expected size. A balance between the accelerating factor of lower viscosity and the retarding factor of smaller clumps might be reached.

I am unable to suggest an explanation for the behaviour of my Blood B.

If the above results are accepted, the conclusions drawn from Day's Pleural Fluid experiments (IXa & 1Xb) must be erroneous. In these experiments varying proportions of pleural fluid (which is often rich in sedimentation producing substances) and citrate solution were added to constant volumes of citrated blood. The sedimentation was observed in Westergren 200 mm. tubes and the log M.V. of the six dilutions plotted against the hypothetical "units of sedimentin" in the various samples. The points fell approximately on a straight line. Assuming that the varying citrate content of the specimens had no effect on their sedimentation rate it therefore appeared that every additional 10% of pleural fluid caused an identical increase in the Log M.V. The two experiments (IXa & IXb) were mathematically correlated to prove that 1 unit of Log M.V. always represented the same quantity of sedimentation producing substances.

But if we take into account the fact that the position of the points on the graph was affected to an unkonwn extent by the varying quantities of

citrate solution in the different dilutions, it is obvious that no definite conclusions can be drawn from these experiments.

In the absence of a completely inert diluting agent a pair of complementary experiments was devised in which a twin series of reconstituted bloods of varying cell volune were set up, one series with the plasma (of the same blood group as the cell donor) of a subject with very slow E.S.R. the other with a constant quantity of the cell donor's rapid plasma and the balance made up of the slow plasma.

EXPERIMENT 9a

To determine the E.S.R. in a series of reconstituted bloods of varying cell volume, each containing the same quantity of plasma from a donor with rapid E.S.R. and with the balance of the specimen made up by varying the quantities of plasma from a donor with very slow E.S.R. The proportion of citrate should be equal in all specimens.

METHOD.

Blood 9 cc. diluted with 3.8% citrate solution 1 cc. was centrifuged and the plasma removed. The cells were washed, and the washed cells suspended in citrate solution (80% cells 20% citrate) From this suspension 5 specimens were prepared, as shown in Table 8, by mixing varying quantities of the cell suspension with a uniform volume of the cell donor's plasma. The volume of the 5 specimens was equalised

by the addition of varying quantities of plasma from a subject of the same blood group with a very slow E.S.R.

TABLE 8

	Cell Suspension		Slow Plasma		Donor's Plasma	
	Cells	Citrate	Plasma	Citrate	Plasma	Citrate
1.	0.56	0.14	-	-	0.64	0.16
2.	0.48	0.12	0.08	0.02	0.64	0.16
3.	0.40	0.10	0.16	0.04	0.64	0.16
4.	0.32	0.08	0.24	0.06	0.64	0.16
5.	0.24	0.06	0.32	0.08	0.64	0.16

The five dilutions were set up in Westergren 200 mm. tubes in the constant temperature chamber and the sedimentation observed at 10 minute intervals for 3 hours.

RESULT: TABLE 9.

Dilution	2nd Hour	M.V.	S.I.	
1.	34.5	35.5	1.55	
2.	58	60	1.78	
3.	76.5	83	1.92	
4.	102	96	1.98	
5.	126.5	120	2.08	

EXPERIMENT 9b

For comparison with experiment 9a to determine the E.S.R. of the same donor's cells in slow plasma only, the citrate volume constant as in Experiment 9a.

METHOD

Blood 9 cc. diluted with 3.8% citrate solution 1 cc. was centrifuged and the plasma removed. The cells were washed, and the washed cells suspended

in citrate solution (80% cells 20% citrate). From this suspension 5 specimens were prepared, as shown in Table 10 by mixing varying quantities of cell suspension with the slow sedimenting citrated plasma used in the last experiment.

TABLE 10

	Cell Suspension		Slow Plasma	
	Cells	Citrate	Plasma	Citrate
1.	0.56	0.14	0.64	0.16
2.	0.48	0.12	0.72	0.18
3.	0.40	0.10	0.80	0.20
4.	0.32	0.08	0.88	0.22
5.	0.24	0.06	0.96	0.24

The five dilutions were set up in Westergren 200 mm. tubes in the constant temperature chamber and the sedimentation observed at 10 minute intervals for 3 hours.

RESULT: TABLE 11.

Dilution	2nd Hour	M.V.	S.I.
1.	13.5	16	1.20
2.	23.5	25	1.40
3.	46.5	45	1.65
4.	71.5	68	1.83
5.	101	111	2.05

The Sedimentin Indices in these two experiments should run parallel, as the difference between each tube in Experiment 9a and its opposite number Experiment 9b is the same quantity of rapid plasma. Chart 7 shows that the sedimentin indices do not run parallel.

CHART 7. RESULTS OF EXPERIMENTS 9a AND 9b.

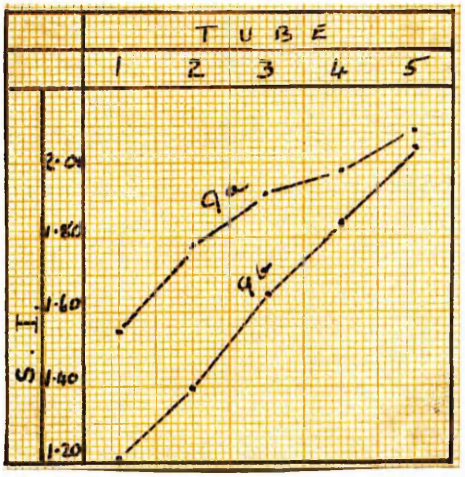
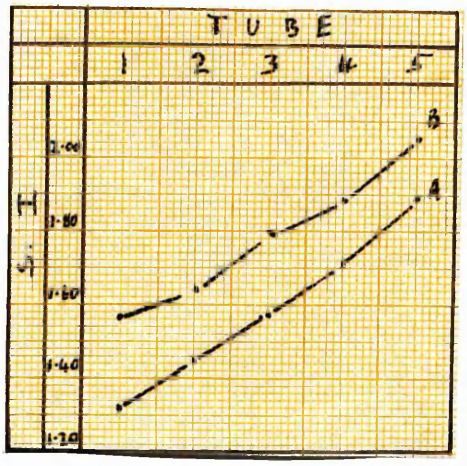


CHART 8. RESULT OF EXPERIMENT 10.



There appeared to be too much chance of experimental error in the above experiments, so a simplified version was evolved. In this the cells of the slow E.S.R. donor were used with his own plasma and with his own plasma plus rapid E.S.R. plasma, or pleural fluid, of the same blood group. In passing it should be noted that, contrary to Day's assertion, the blood group is as important when pleural fluid is used as when plasma is used. The pleural cavity can be a wonderful reservoir of typing serum which, in a case investigated by Cutbill and myself, was of high titre.

EXPERIMENT 10.

Object: To determine the increase in E.S.R. in a series of reconstituted bloods resulting from the replacement of plasma causing slow E.S.R. by an equal quantity of plasma or pleural fluid causing rapid E.S.R.

METHOD.

13.5 cc. slow sedimenting blood diluted with 1.5 cc. of 3.8% citrate solution was centrifuged and the plasma removed. The cells were suspended in citrate solution to form an 80% suspension. 5 cc. citrated pleural fluid (4 fluid to 1 citrate) of the same blood group was obtained, or alternatively citrated plasma from a subject with rapid E.S.R. The citrate concentration in the constituents of the reconstituted bloods was therefore approximately equal.

Ten dilutions were prepared as set out in Table 12.

TABLE 12.

Series A.	1	2	3	4	5
Cells	0.8	0.7	0.6	0.5	0.4
Plasma	0.8	0.9	1.0	1.1	1.2
Series B.	**1**	**2**	**3**	**4**	**5**
Cells	0.8	0.7	0.6	0.5	0.4
Slow Plasma	-	0.1	0.2	0.3	0.4
Pleural Fluid or Rapid Plasma	0.8	0.8	0.8	0.8	0.8

The ten dilutions were set up in Westergren 200 mm. tubes in the constant temperature chamber and the sedimentation observed at 10 minute intervals for 3 hours. The results are tabulated below and are shown graphically on Chart 8.

RESULT: TABLE 13.

Sedimentin Indices

Dilution No.	1	2	3	4	5
Series A.	1.32	1.45	1.57	1.71	1.88
Series B.	1.57	1.65	1.79	1.89	2.05
Differences.	0.25	0.20	0.22	0.18	0.17

DISCUSSION

According to Day's hypothesis the difference between each tube in Series A and its opposite number in Series B is N "units of sedimentin", as equal quantities of slow plasma have been replaced by rapid plasma in the five tubes of Series B. Therefore the difference between the Sedimentin Indices of each pair of tubes should be the same.

This result was not obtained. There was a tendency for the Sedimentin Indices to converge as the S.I. increased, though this was less marked than in the less accurate experiment which preceeded. Therefore it cannot be assumed that the Sedimentin Index has an absolute value.

In practice the Sedimentin Index exaggerates small changes in E.S.R. within the limits of experimental error, at the lower rates, and minimises changes at the rapid rates.

For example:-

M.V.	S.I.	M.V.	S.I.
4	0.60	40	1.60
6	0.78	60	1.78

From a long experience of the erythrocyte sedimentation test I am convinced that a change from M.V. 4mm/100 min. to M.V. 6mm/100 min. may have no clinical significance, while a change from M.V. 40mm/100 min. to M.V. 60mm/100 min. is definitely significant. The change in S.I. is the same in the two cases.

THE CUTBILL INDEX.

Cutbill, using the Westergren technique, found that there was a lack of correlation between the 1st and 2nd hour readings. He therefore temporarily abandoned them in favour of a graph recording the fall of the upper corpuscular layer hourly for five hours and then at 24 hours (see Chart 9). This was fairly satisfactory for serial tests in a single patient, but it is not good for the comparison of one patient with another. In order to do this he evolved a method of expressing the 5 hour graph as a single figure (Cutbill 1939). The five hour period was chosen because it includes all three phases of sedimentation, acceleration, maximum velocity and packing, in all but the slowest bloods.

The hourly readings are read as percentages of the blood column (2 mm- 1%) and plotted on a time distance graph. The area above the line is calculated by the trapezoid rule and expressed as a percentage of the rectangle bounded by the ordinate, height of column, and the abcissa time. In practice this is quite simple, as is shown by this example.

Time (Hrs.)	Fall%	Multiplier	Result.
0	0	1	0
1	43	2	86
2	63	2	126
3	65	2	130
4	66	2	132
5	67	1	67
			54.1%

For convenience the decimal point was omitted and the above results would have been expressed as C.I. = 541.

The method was clinically satisfactory, but was laborious, as are all methods involving plotting and calculation. It was not abandoned until the close numerical relationship between the Cutbill Index and the 2nd hour reading was proved. This is demonstrated in Chart 10. My personal experience of this method lasted more than a year (over 2,5000 tests).

CHART 9.

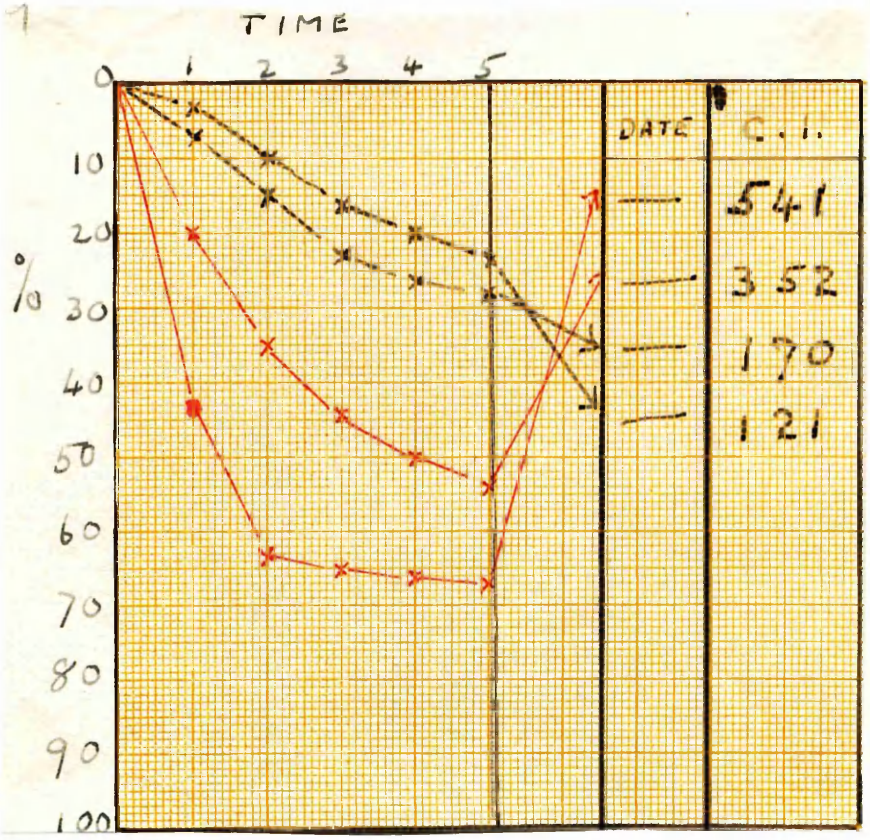
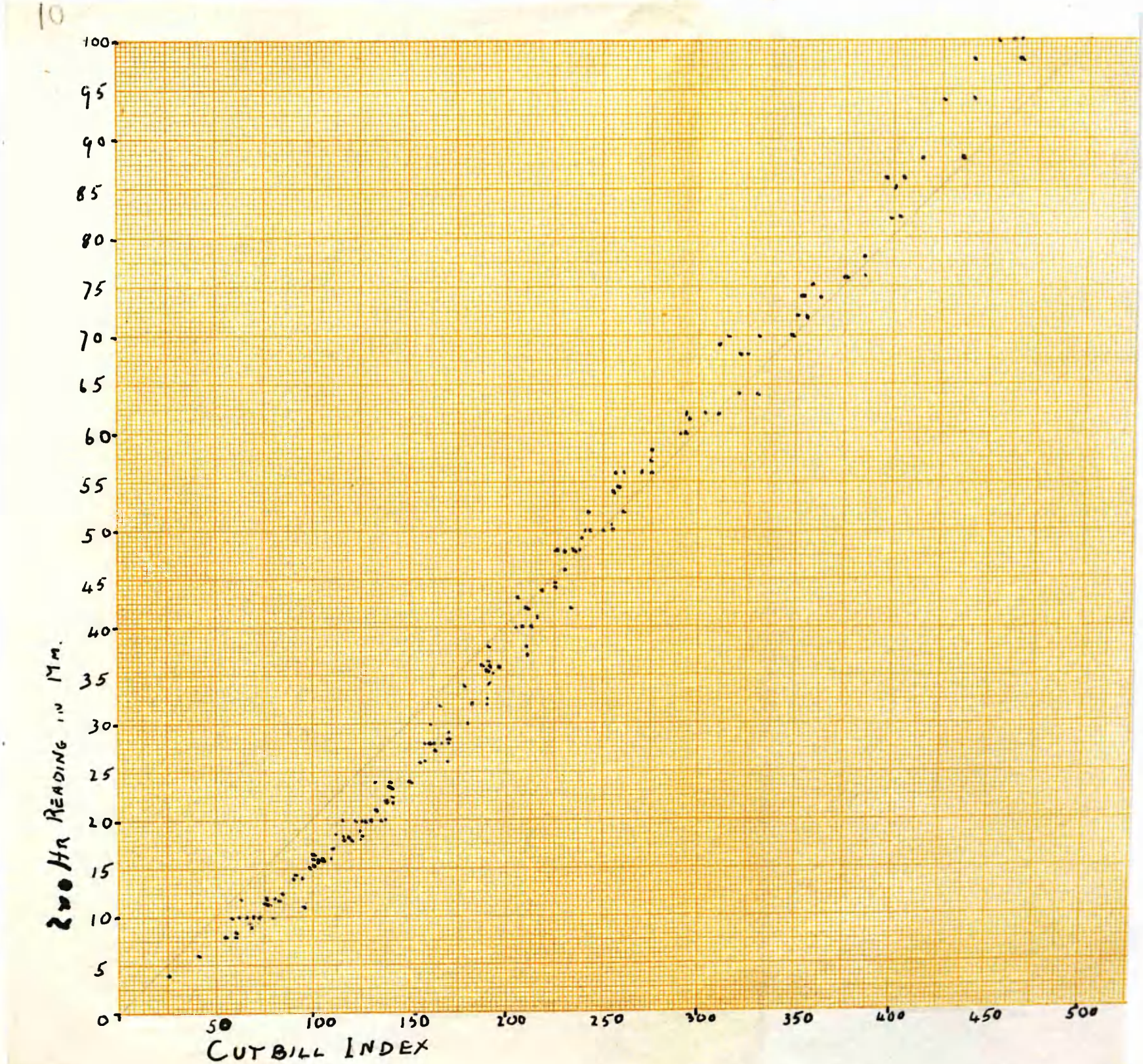


CHART 10.


10
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
2 HR READING IN MM.
50
100
150
200
250
300
350
400
450
500
CUTBILL INDEX

CHOICE OF TECHNIQUE.

In selecting a method of estimating the E.S.R. for routine use in an institution where serial tests are carried out, it must be remembered that any of the many methods that have been devised will give useful results, though the sensitivity varies greatly.

The word sensitivity as used here requires definition. It indicates:-

1. That the E.S.R. by the method used bears roughly the same proportion to the maximum velocity of sedimentation at all rates.

2. That the scale of readings is large enough to prevent experimental error being confused with significant changes in E.S.R.

For example, when a short column is used cell packing causes deceleration before the maximum velocity is reached and results for the higher rates are smaller, in proportion to the M.V., than results for slow and medium sedimenting bloods. So there is lack of sensitivity at higher rates.

When readings are taken at $\frac{1}{2}$ hour and 1 hour most of the slow sedimenting bloods are still in the acceleration phase, and results for the slower sedimenting bloods are smaller in proportion

to the M.V. than results in the medium and higher rates, and the method lacks sensitivity for slow sedimenting bloods.

A method employing a short column with the reading taken at ½ hour may give results which are roughly proportional to the M.V. because the acceleration and deceleration phases overlap and sedimentation is always slower than the theoretical maximum velocity. But the interval between the fastest and slowest rates is small, and sensitivity is poor for all rates.

Of the standard test tubes or pipettes, the Westergren pipette approaches most closely to the ideal. The height of column is sufficient, and the bore is adequate if citrated blood is used. And it is convenient to use a technique that is used more than any other in Europe.

On theoretical gounds, the maximum velocity of sedimentation should be measured. To estimate this the fall of the upper corpuscular layer is plotted at 5 or 10 minute intervals on a time/distance graph. The maximum gradient section of the curve is extended and from this line the maximum velocity of sedimentation (M.V.) is found. Day's method of expressing this in millimetres per 100 minutes is easy to measure and avoids trouble with the decimal point. However, the estimation of M.V. is a time consuming procedure. One person

cannot take the readings accurately on more than 10 to 12 tubes, and he has to do this for at least two hours - longer if there are slow sedimenting bloods. There is not time to settle to other work in the interval between readings. After that the plotting and measurement of M.V. takes a further two minutes per specimen. It should be noted that the determination of the maximum gradient is not always easy, especially when the upper corpuscular layer is indefinite. Minor kinks may then appear in the curve and some discretion must be used in drawing the line of maximum gradient. If discretion is not used the experimental error may be considerable.

Because of the difficulty of estimating the M.V. when dealing with a large number of tests, the method has been used by only a few workers, but it has a good claim to be used as the standard by which other methods are judged.

Users of the Westergren technique commonly report the distance fallen by the upper corpuscular layer in one hour. But large discrepancies between the fall in 1st and 2nd hours led to the introduction of the Cutbill Index at the Cheshire Joint Sanatorium. Later the close relationship between the Cutbill Index and the fall in 2 hours was observed. I have now undertaken the comparison of the fall in 1 hour and 2 hours with the M.V. (See Charts 11 & 12).

50 A

CHART II.

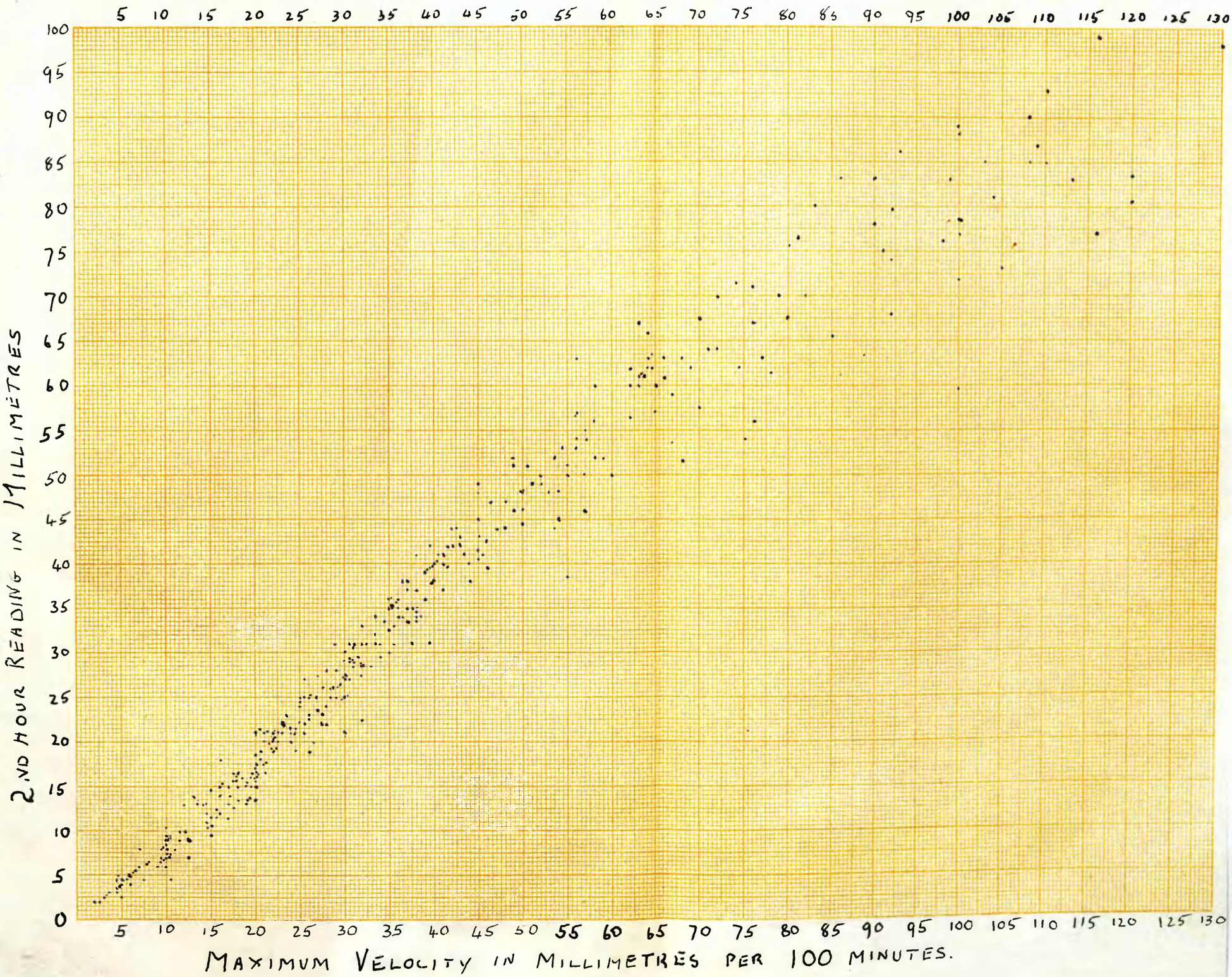
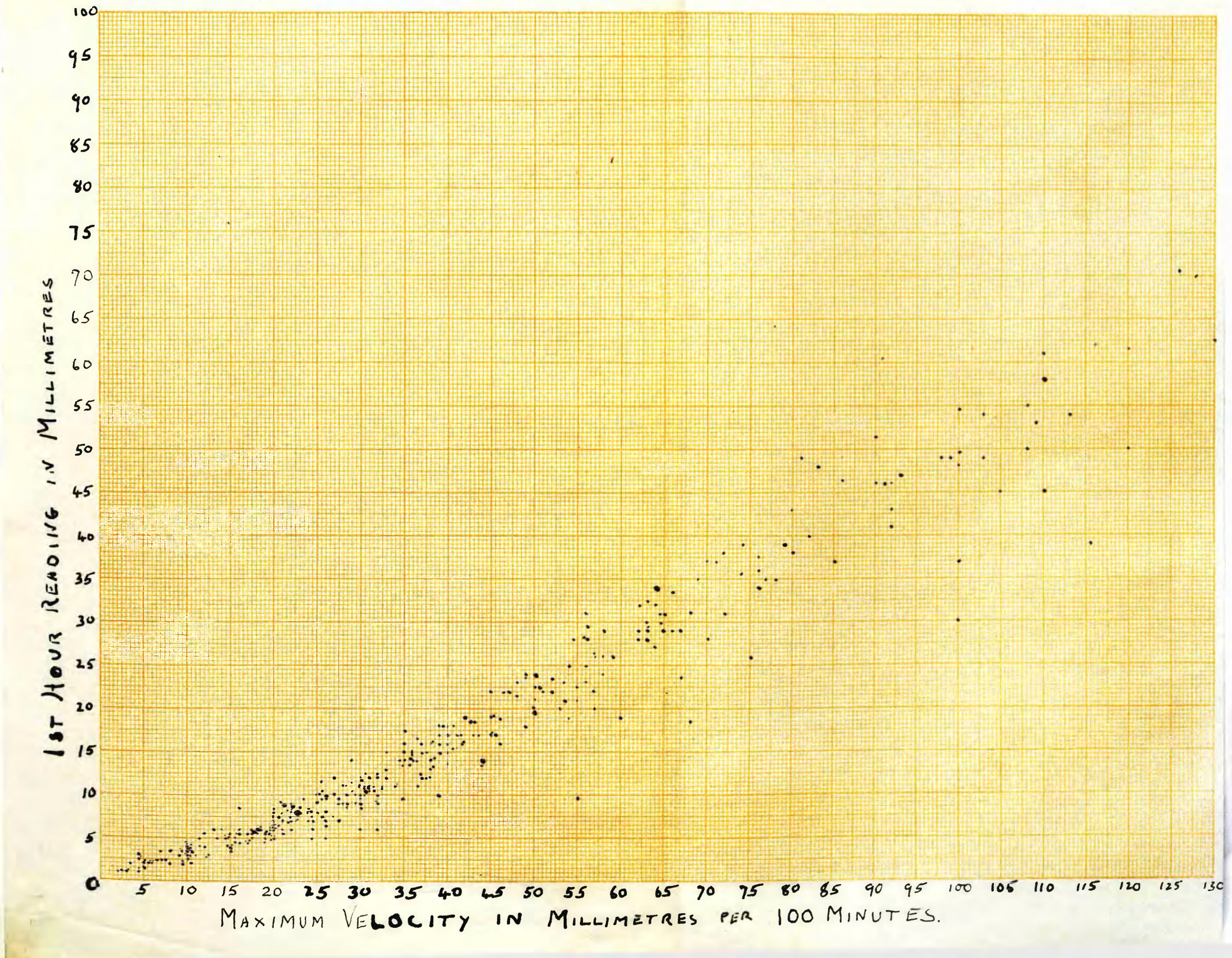

2.ND HOUR READING IN MILLIMETRES
MAXIMUM VELOCITY IN MILLIMETRES PER 100 MINUTES.
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130

CHART 12.


100
95
90
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80
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40
35
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5
0
1ST HOUR READING IN MILLIMETRES
5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130
MAXIMUM VELOCITY IN MILLIMETRES PER 100 MINUTES.

There is close correlation between the fall in 2 hours and the M.V. up to an E.S.R. of 50mm/2 hours. For rates above this the scatter on the graph is considerable and increasing. Some of the higher readings were not accommodated on the graph and were as follows:-

TABLE 14.

2nd Hour	M.V.	2nd Hour	M.V.	2nd Hour	M.V.
106	128	120	212	106	140
110	320	126	180	85	200
92	183	68	140	106	140
106	126	94	164	104	174
131	220	105	161	101	150
100	168	106	175	108	230
93	205	85	200	89	138
100	132				

The accommodation of 6% more points did not warrant quadrulping the size of the graph.

The most inconsistent spot on the graph 2 hour 59.5, M.V. 100, belonged to the syphilitic patient referred to in Part III. The results of all other estimations on this patient showed excessive scatter, but were off the graph and appear in the above table.

In comparison, the correlation between the fall in 1 hour and the M.V. was not so good. The horizontal scatter at 5mm/1 hour was 15 mm. compared with a scatter of 5 mm at 10mm/2 hour. There is excessive scatter in the 1st hour graph at all comparable levels until the level on the

2nd hour graph is reached where scatter becomes considerable.

Comparing the 1st and 2nd hour readings in this series directly it was noted that in the lower range of E.S.R., especially under 30mm/ 2 hour, the 2nd hour reading is much more sensitive than the 1st hour reading. In this range the 1st hour reading is frequently nearer $\frac{1}{3}$ than $\frac{1}{2}$ of the 2nd hour reading, because in slow sedimenting bloods, the first hour includes only the acceleration period of the sedimentation. The following are examples, and a sedimentation graph demonstrating this point is attached (Chart 13)

TABLE 15.

1st Hour	2nd Hour	M.V.	1st Hour	2nd Hour	M.V.
1	3	4.5	8.5	24	28
2	6.5	9.5	10.5	25	25.5
3	7.5	10	11	31	35.5
3.5	9.5	10.5	12	30	30
5	15.5	20	12	34	38
6	19	22	12.5	35	37
7	19	22	14	36	36

On the other hand, for very rapidly sedimenting bloods the first hour reading is more sensitive than the second hour reading, because the maximum velocity period is during the first hour when the E.S.R. is rapid, and deceleration due to packing occurs during the second hour, as is seen from these examples and the sedimentation graph (Chart 14).

CHART 13.

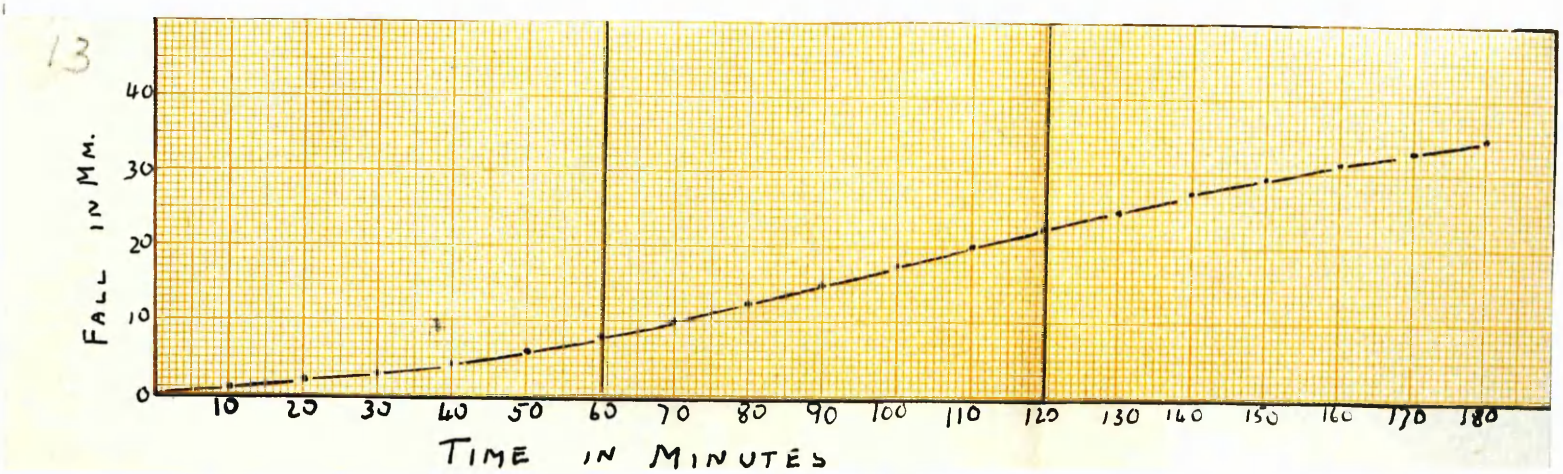


CHART 14.

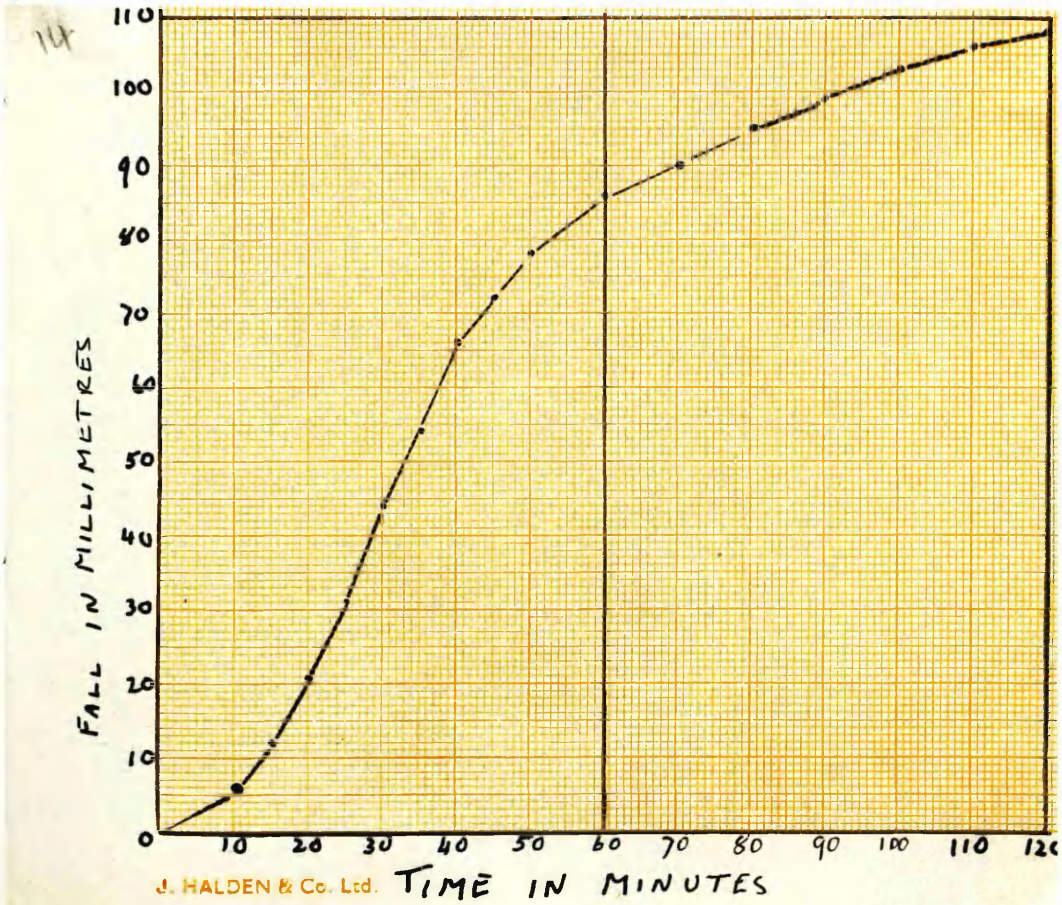


TABLE 16

1st Hour	2nd Hour	M.V.	1st Hour	2nd Hour	M.V.
61	93	110	96	110	320
65	89	138	96	120	212
69	106	140	97	126	180
77	92	183	101	132	220
86	108	230			

Less than 20% of the results in this unselected series of estimations are above the level at which the 1st hour reading may be considered more accurate, while more than 50% are below the level at which the 2nd hour is more accurate.

From the point of view of a clinician I find that accuracy of E.S.R. is more desirable in the slower range of E.S.R. than in the more rapid range as it is usually in the patients with moderate to slow E.S.R. that one finds normal temperature and pulse rate, insignificant changes in physical signs from month to month, and equivocal radiological changes. In patients with unilateral disease treated by artificial pneumothorax, pulse rate, temperature, physical signs and skiagram may all fail to give information as to the progress of the tuberculous lesion. In these cases the return of the E.S.R. to normal levels and its maintenance there is probably the best indication of the time for discharge from the sanatorium. The second hour reading is more sensitive than the first hour reading

for this purpose. The tolerance for exercise has, of course, been proved, by the graduated work and exercise of sanatorium routine.

It is therefore suggested that sedimentation in the Westergren tube should be read at two hours, and that additional information regarding rapidly sedimenting bloods will be gained if it is read at one hour also.

SUMMARY OF SUGGESTED TECHNIQUE

1. 20% of 3.8% sodium citrate solution should be used as anticoagulent.
2. The Westergren pipette should be used.
3. The Temperature of the test should be controlled.
4. Readings should be taken at 1 hour and 2 hours.
5. Correction for cell volume is not essential when serial tests are performed.

PART III

I N T R O D U C T I O N

In order to show how the method of estimating and recording the Erythrocyte Sedimentation Rate advocated at the end of Part II works out in practice, I have selected a series from cases under my care during the past five years.

They are chosen as typical of the close relation between the E.S.R. and the clinical progress of cases treated by a variety of methods, and examples are also given of anomalous results due to various causes. A short note on each case accompanies the progress chart which shows the E.S.R. at 28 day intervals, the landmarks of treatment, complications, the state of the sputum, and sketches of some skiagrams.

There has of recent years been a tendency among tuberculosis workers to abandon the assistance of serial E.S.R. estimations in assessing the progress of patients, while still using the test as an aid to diagnosis and prognosis. The authors of one recent paper (Lewis-Fanning & Myers 1942) contend that too many extraneous factors may cause fluctuation in the E.S.R. from time to time, yet they prove statistically, as did Traill (1933), that a single estimation on

discharge from a sanatorium is of considerable prognostic value. My own view is that the extraneous factors are more easily recognised in serial tests, and an explanation for most anomalous results can be discovered. I have also been associated with some unpublished work which shows that prognosis from serial tests is much more accurate than prognosis from a single test.

The following abbreviations are used on the charts.

R.A.P.	= Right Artificial Pneumothorax
L.A.P.	= Left Artificial Pneumothorax
J.	= Internal Pneumolysis
⌀	= Phrenic Evulsion
T.	= Thoracoplasty
G.	= Gold treatment commenced
Ca.	= Calcium Gluconate Treatment commenced.
SP.	= Sputum.
+	= T.B. found on direct smear
-	= No T.B. found on direct smear
C	= Result of Culture for T.B.
M	= Tuberculin Test
End	= Tubercle Endotoxoid.

PRIMARY TUBERCULOUS INFECTION

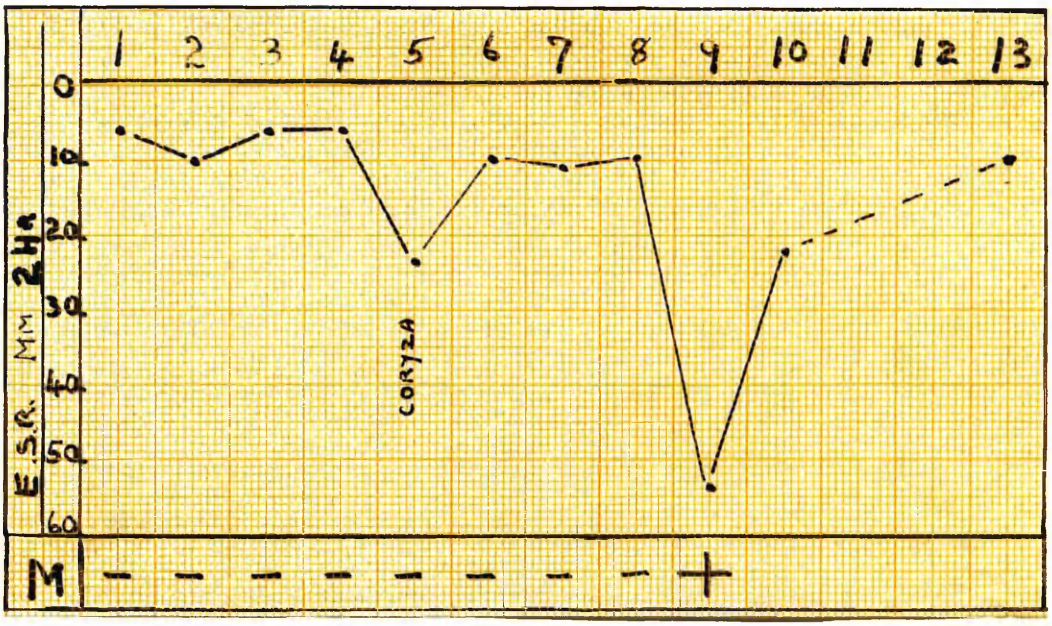
The effect of Primary Tuberculous Infection on the E.S.R. is demonstrated by the following three nurses who joined the staff with a negative Tuberculin reaction. The Tuberculin reaction and E.S.R. were repeated monthly as long as the former remained negative. Thereafter the frequency of E.S.R. estimation and radiological examination depended on the clinical condition.

Case 1. This case shows a sudden sharp rise in E.S.R. coincident with the change in Tuberculin reaction, accompanied by no radiological or symptomatic evidence of tuberculous infection. The rapid return of the E. S.R. to normal limits is noteworthy.

Case 2.

This case shows a significant rise in E.S.R. coinciding with the change in Tuberculin reaction, and the appearance of a typical primary complex in the Right Lung. A small lesion at the right base was accompanied by enlargement of right hilar glands. There were no symptoms, and the E.S.R. fell to a level within normal limits. There was rapid retrogression of the hilar glands and the parenchymal lesion is contracting.

CASE 1.


1 2 3 4 5 6 7 8 9 10 11 12 13
0
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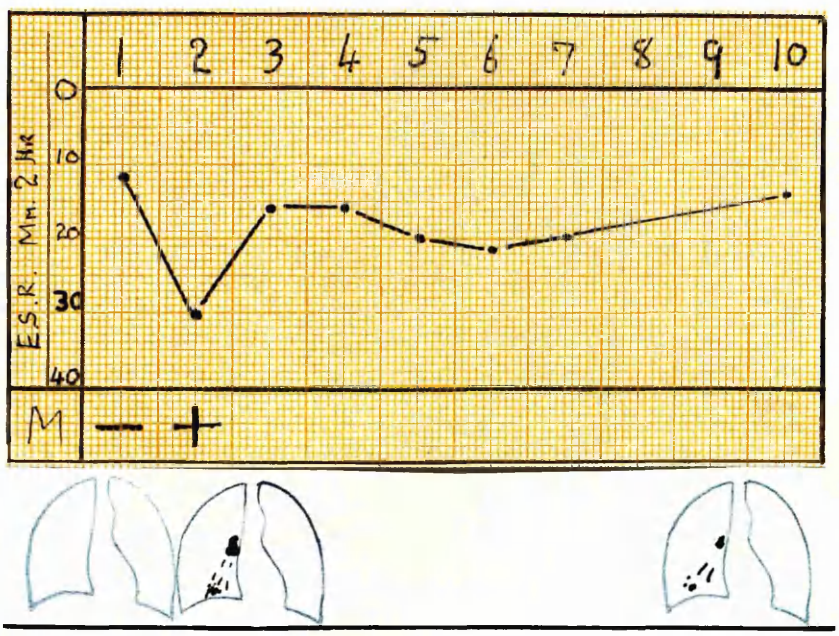
30
40
50
60
E.S.R. MM 2Hs
CORYZA
M
- - - - - - - - +

CASE 2.

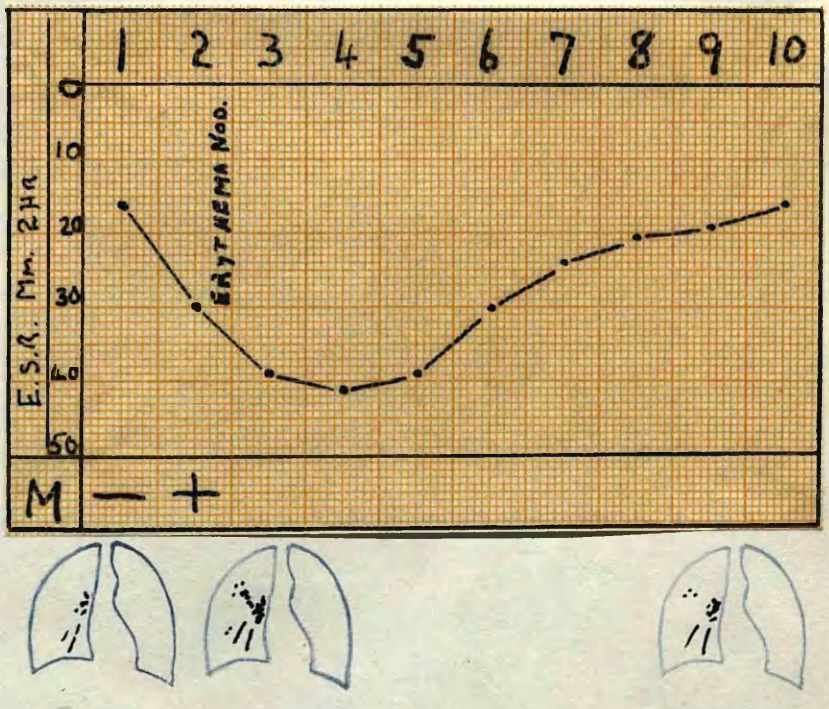

1 2 3 4 5 6 7 8 9 10
0
10
20
30
40
E.S.R. MM. 2 HR
M
- +

Case 3.

This case shows a significant sustained rise in E.S.R. commencing with the change in Tuberculin reaction, which was accompanied by Erythema Nodsum, elevated temperature and increased pulse rate, and radiological appearance of a typical primary complex in the Right Lung, though this gave rise to no localising symptoms or physical signs.

She was off duty for four months, and was still on half time when she left the staff seven months after the change in Tuberculin reaction. The E.S.R. had returned to normal and the radiological appearance was much improved.

CASE 3.



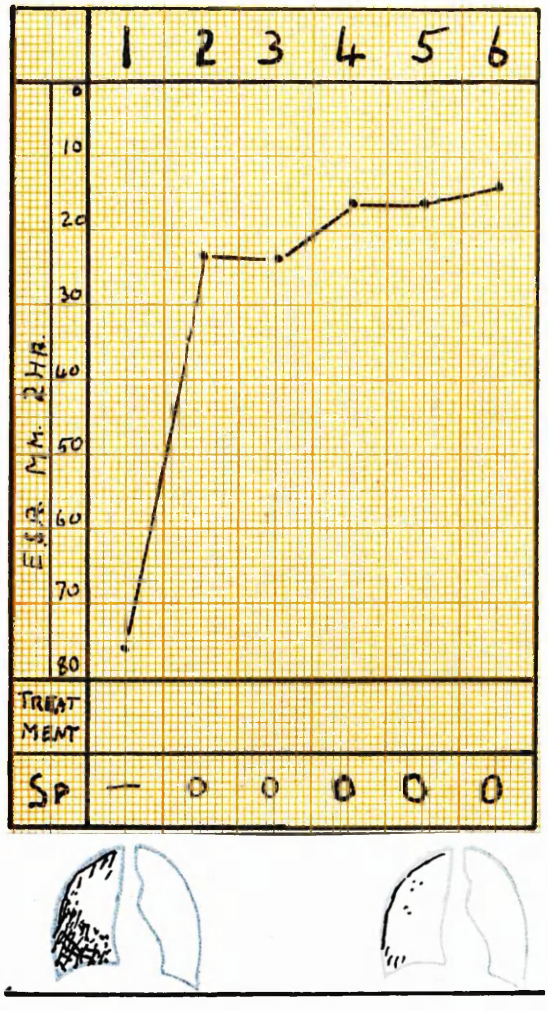
PLEURISY WITH EFFUSION

Case 4 (B.P.)

Admitted in fair general condition with a history of pleurisy 3 months before and again 6 weeks later. After the second attack fluid was aspirated from the right chest in hospital. On admission here she was symptomless, but the skiagram showed a fluid opacity at the right base and poor translucency throughout the right chest. An attempt to aspirate fluid for bacteriological examination failed.

Progress was uneventful. Her weight increased by 21 lbs in 12 weeks, and good radiological clearing accompanied the rapid return to normal of the E.S.R. Traill found that the prognosis was very good in cases of pleurisy with effusion who received sanatorium treatment until the E.S.R. was normal.

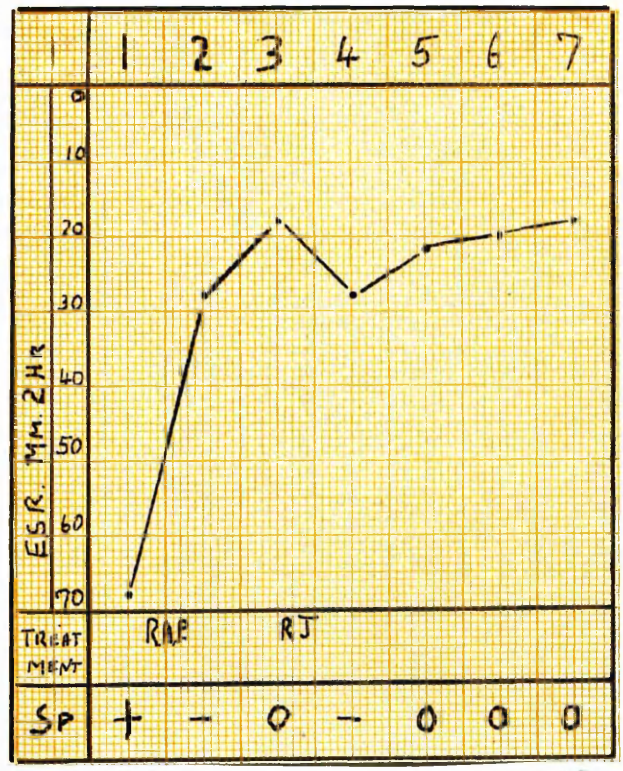
CASE 4.



Case 5 (M.B.)

Admitted in fairly good general condition with a history of an influenza-like illness 6 months before admission, and recurrence of cough, sputum and malaise and chest pain three months later. The sputum was blood-streaked once. The skiagram showed exudative mottling of the right upper lobe with a honeycomb of small cavities. There was some mottling in the right lower lobe and in the left mid zone (? apex of lower lobe) A right artificial pneumo-thorax was induced, and all adhesions were cauterised 9 weeks later. The reaction to the cautery shows well on the E.S.R. chart. Thereafter her progress was uneventful.

CASE 5.


1 2 3 4 5 6 7
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20
30
40
50
60
70
ESR. MM. 2 HR
TREAT MENT
RMP
RJ
SP
+ − O − O O O

BILATERAL PNEUMOTHORAX

Case 6 (N.M.)

Admitted in fair general condition, having been in another Sanatorium for most of the previous year. The only symptoms were slight cough and malaise. The skiagram showed infiltration and a cavity in the right mid-zone and a similar lesion in the left sub-apical region.

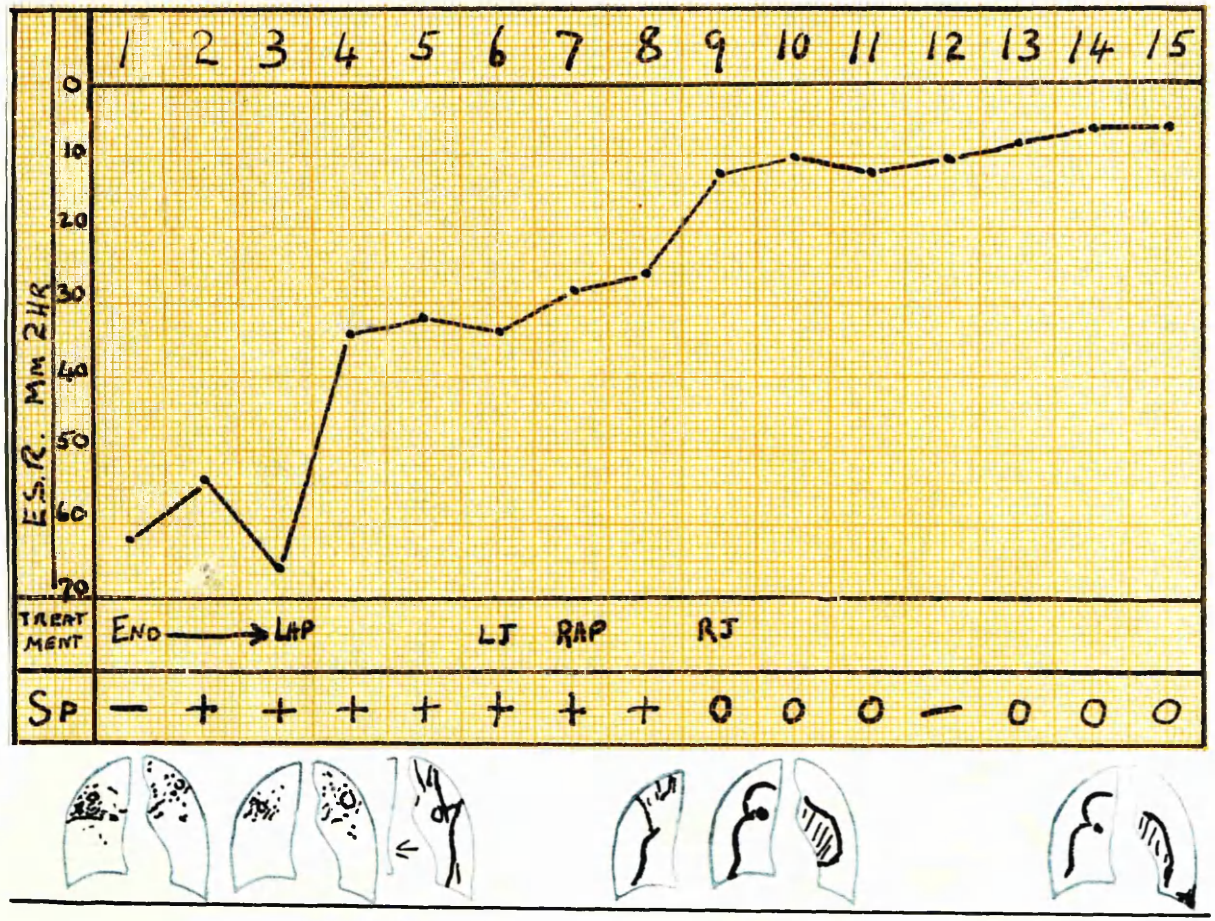
Artificial pneumothorax treatment was with-held at first because of the minimal symptoms and negative sputum. But a skiagram at 3 months showed spread of the disease in the left lung, and the sputum was positive. Improvement commenced after induction of a left A.P. and continued with the stages of treatment. By the 9th month she had a good bilateral pneumothorax, free from adhesions, no sputum and a normal E.S.R. Further progress was unaffected by the appearance of a transient effusion in the left A.P. which cleared up after three aspirations without adversely affecting the pneumothorax.

PLEURAL EFFUSION IN ARTIFICIAL PNEUMOTHORAX

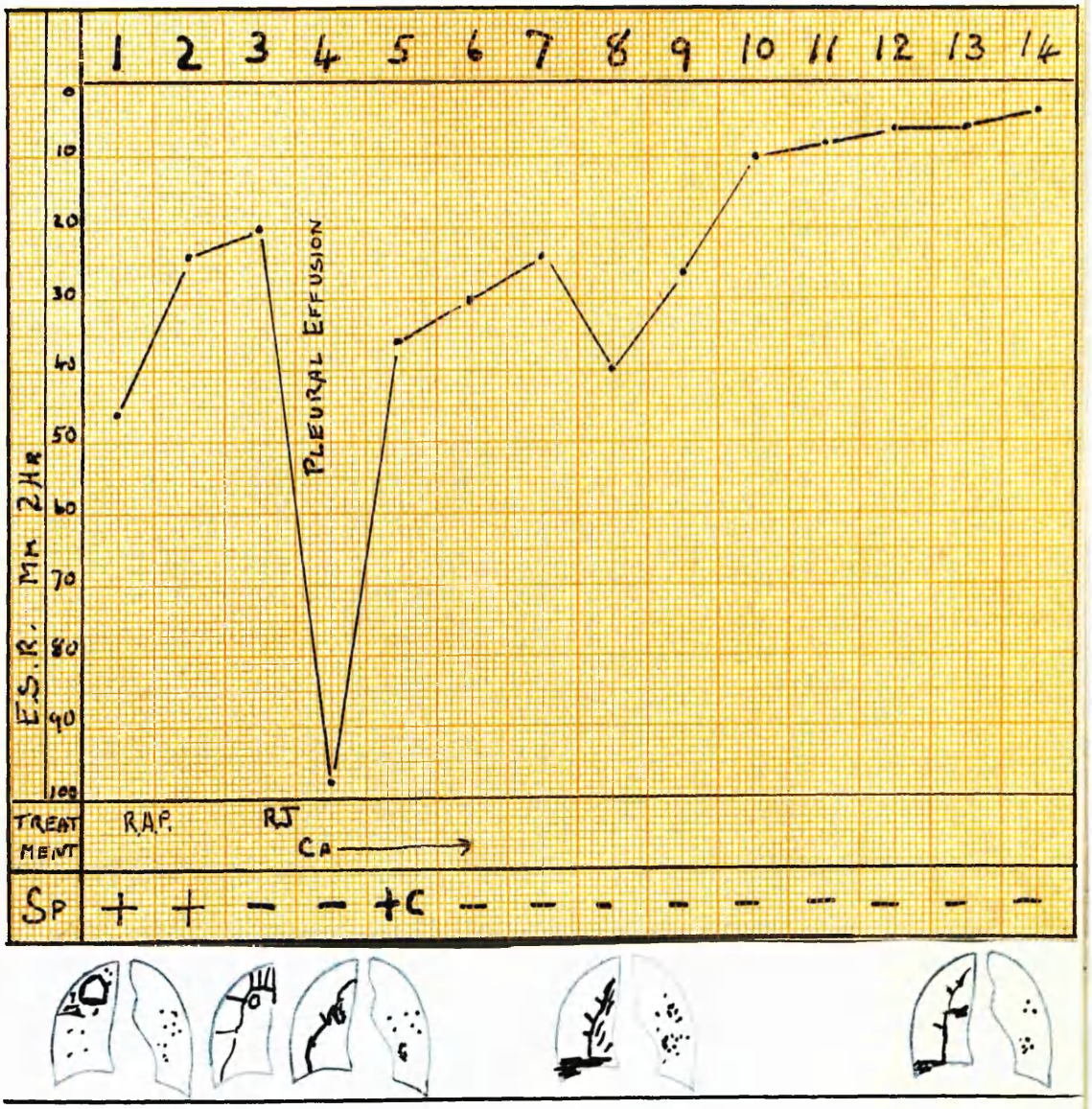
Case 7 (A.S)

Admitted in fair general condition, with a history of asthma for 11 years. Malaise commenced 18 months before admission though the asthma was better. Chest pain, anorexia and loss of weight commenced 6 months later, when the sputum was positive for tubercle bacilli. Two months later all symptoms were worse and he entered another sanatorium where he remained until he came to us, having two haemoptyses during his stay there. The skiagram showed a large cavity with fluid level in the right upper lobe, surrounded by exudative mottling, and there was exudative mottling in the left mid zone. A right artificial pneumothorax was induced and six weeks later adhesions were cauterised. There was a febrile reaction after this operation and a massive pleural effusion formed. This was aspirated fifteen times before it dried up, leaving an effective pneumo-thorax with the cavity closed. The deterioration in E.S.R. at the 8th month coincided with a slight spread of the disease in the left lung. This cleared considerably before discharge.

CASE 6.


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
0
10
20
30
40
50
60
70
E.S.R. MM 2HR
TREAT MENT
END → LAP
LJ RAP RJ
SP
— + + + + + + + 0 0 0 — 0 0 0

CASE 7.


1 2 3 4 5 6 7 8 9 10 11 12 13 14
E.S.R. MM. 2HR
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10
20
30
40
50
60
70
80
90
100
PLEURAL EFFUSION
TREAT MENT
R.A.P.
R.T.
C.A.
Sp
+ + - - +C - - - - - - - - -

ARTIFICIAL PNEUMOTHORAX WITH PLEURAL EFFUSION

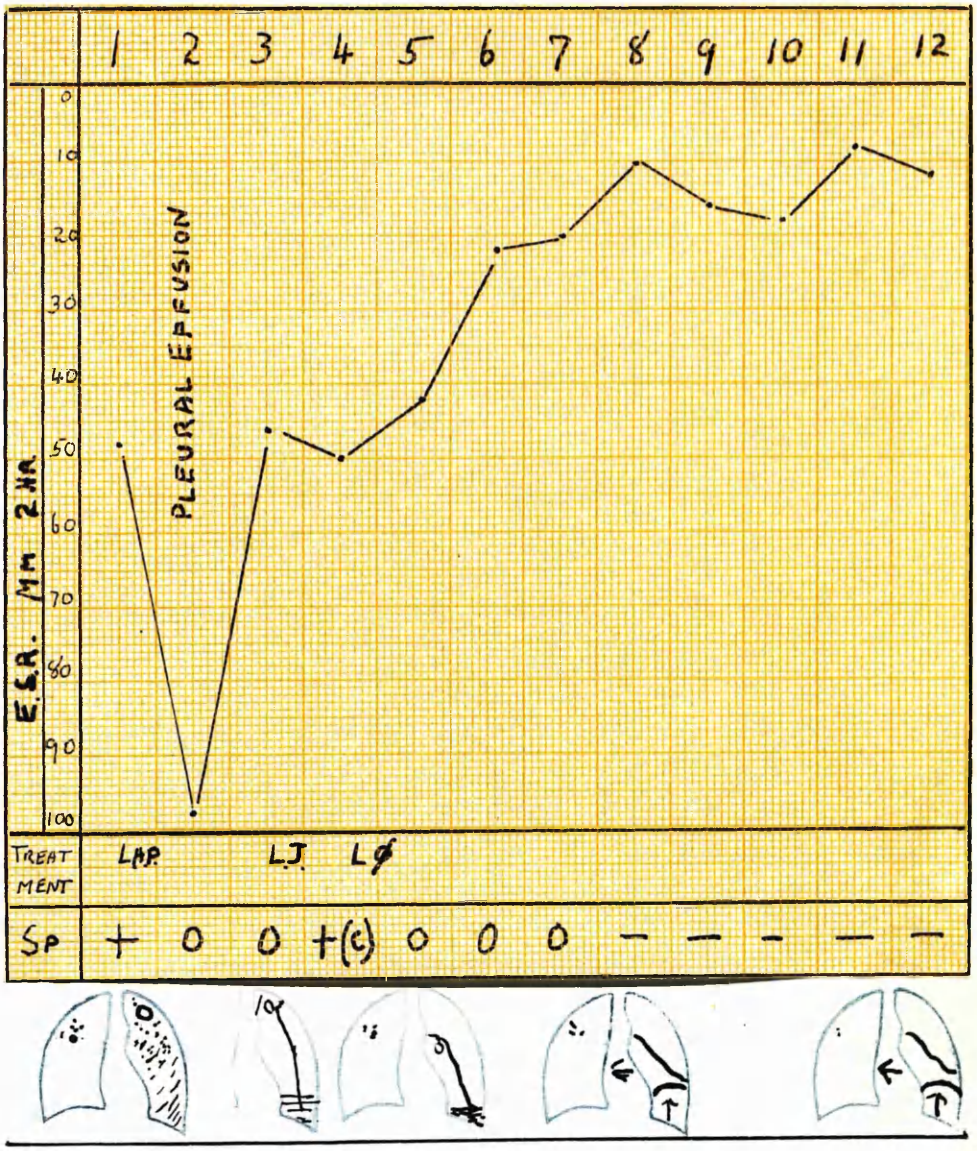
CASE 8 (H.C.)

Admitted in fairly good general condition, though febrile, with a history of loss of weight for four months and recent cough, chest pain, haemoptysis and dyspnoea. The skiagram showed slight scattered mottling in the right lung. On the left there was a large cavity near the apex and a small pleural effusion at the base. A left artificial pneumo-thorax was induced and a month later 10 ounces of clear fluid was aspirated from the left chest. Thereafter the temperature settled, and adhesions were cauterised in the 3rd month. As the cavity did not close although the apex was completely free, the left phrenic nerve was evulsed in the 4th month. From then onwards her progress was uneventful.

This case and the previous one demonstrate that in cases of pleural effusion complicating artificial pneumothorax, a rapid improvement in the E.S.R. indicates probable resolution of the effusion, though this may take a considerable time. If, on the other hand, the E.S.R. remains rapid after an effusion has developed, the effusion is likely to progress to empyema formation.

These findings have been observed in a large number of cases, though all are not so clear cut.

CASE 8.


1 2 3 4 5 6 7 8 9 10 11 12
0 10 20 30 40 50 60 70 80 90 100
E.S.R. MM 2HR.
PLEURAL EFFUSION
TREAT MENT
LAP. LJ. LØ
Sp + 0 0 +(c) 0 0 0 − − − − −

ARTIFICIAL PNEUMOTHORAX WITH PLEURAL EFFUSION

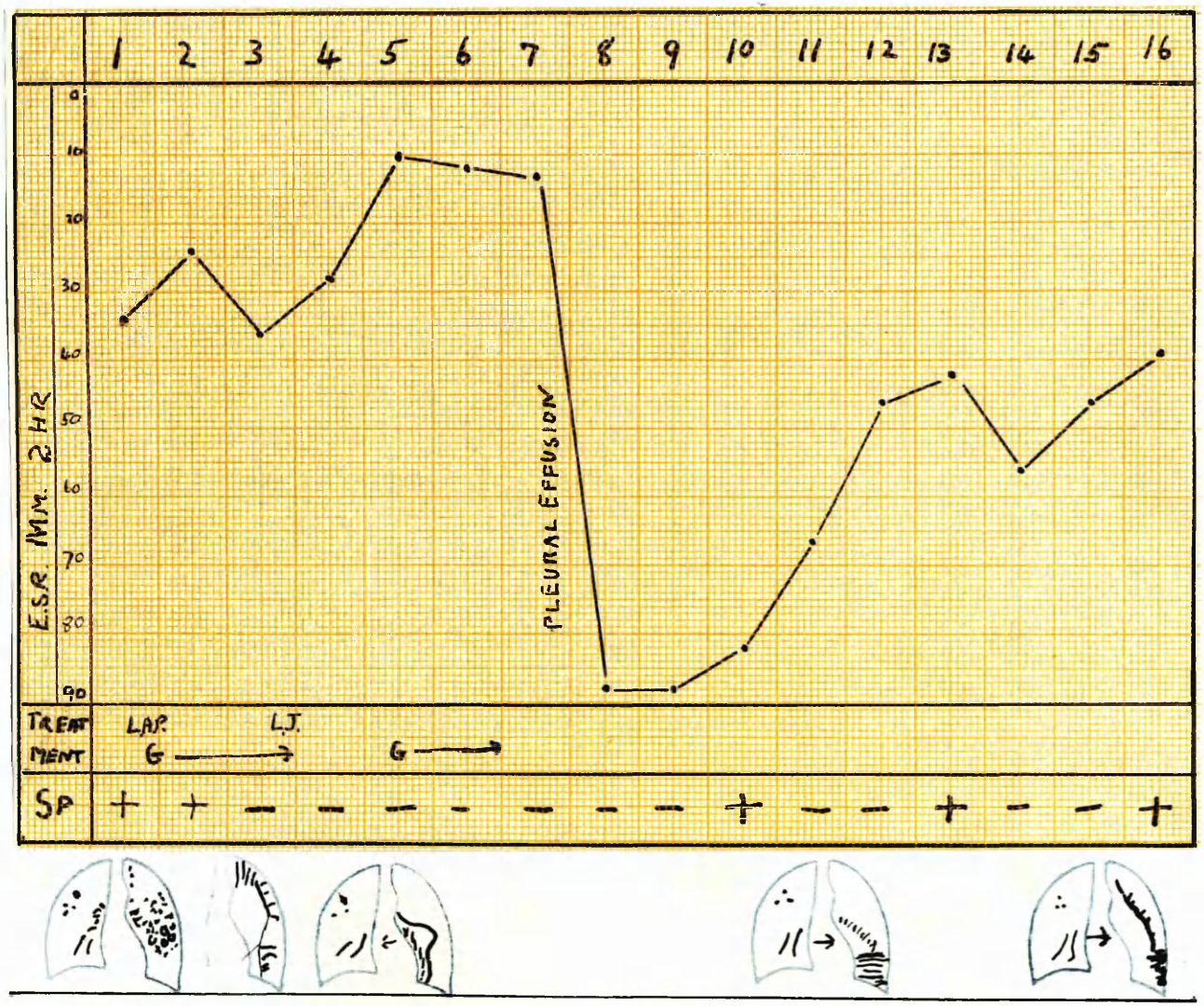
Case 9 (J.W.)

In contrast to the two previous cases this is an example of pleural effusion going on to empyema. He was admitted in fair general condition with a history of morning cough commencing a year earlier. Three months later there was cough, copious sputum, huskiness, dyspnoea, chest pain, malaise, and a large haemoptysis. After discharge from military hospitals it was some time before he could be persuaded to enter a sanatorium. The skiagram showed a small Assmann's focus and slight mottling in the right mid-zone, and in the left heavy mottling mainly exudative in type, in the mid-zone, and a group of cavities. A left A.P. was induced and intra muscular gold injections commenced. Eight weeks later all adhesions in the A.P. were successfully cauterised. The reaction of this extensive burn was of short duration and he made good progress for three months. A pleural effusion developed with acute onset and high temperature in the 8th month. The fluid was clear at first but the tubercle bacillus was recovered on culture. The temperature began to fall slowly after the first week but did not reach normal levels, and there was a febrile reaction

to every aspiration of fluid, which became frankly purulent after 8 weeks. After months of treatment by pleural lavage and intrapleural instillation of cod liver oil the empyema cavity is slowly obliterating, but with the re-expansion of the left lung, which commenced early in the course of the effusion the sputum again became positive.

The persistently rapid E.S.R. in the 8th 9th and 10th months should be contrasted with the rapid improvement in E.S.R. after on month in the two previous cases in which the effusion cleared up without becoming purulent. The presence of tubercle bacilli in the fluid does not exclude the possibility of a satisfactory outcome.

CASE 9.


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
E.S.R. MM. 2 HR
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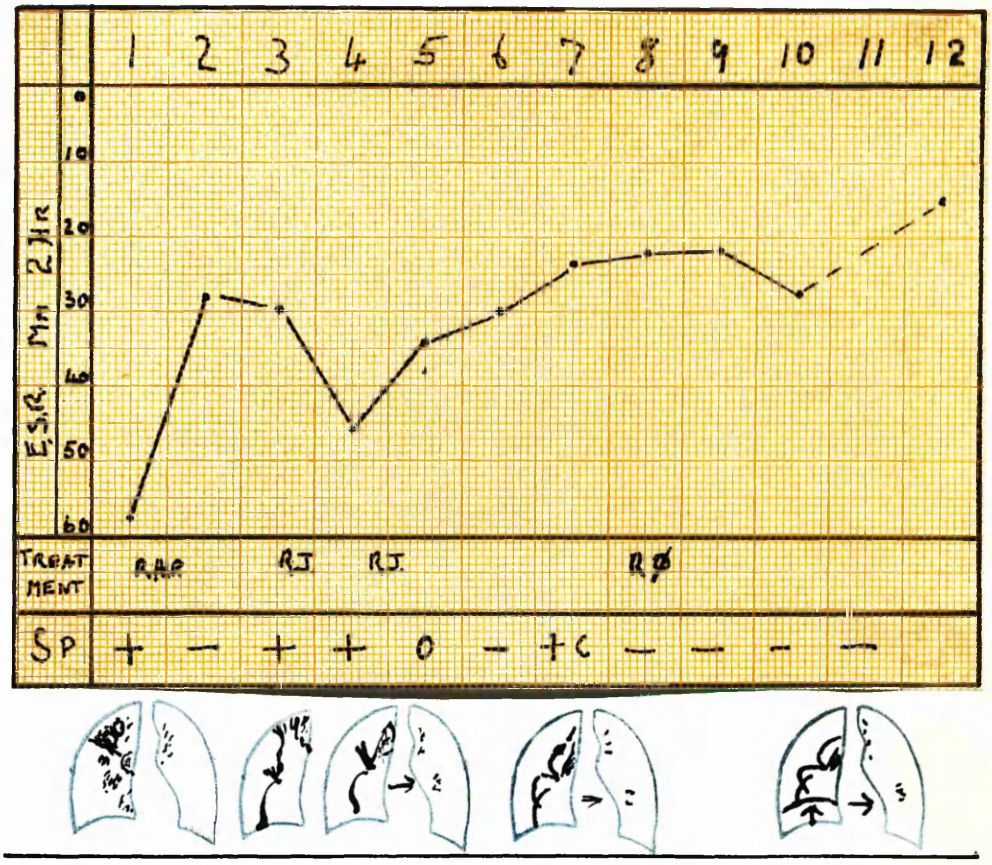
90
PLEURAL EFFUSION
TREAT MENT
LAP.
G
L.J.
G
SP
+ + − − − − − − − + − − + − − +

CASE 10.


1 2 3 4 5 6 7 8 9 10 11 12
E.S.R. Mm 2 Hr
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30
40
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60
TREAT MENT
R.H.P
R.J
R.J.
R.Ø
SP
+ − + + 0 − +C − − − −

PULMONARY TUBERCULOSIS COMPLICATED BY DIABETES MELITUS TREATED BY ARTIFICIAL PNEUMOTHORAX AND PHRENIC EVULSION

Case 10 (H.S.)

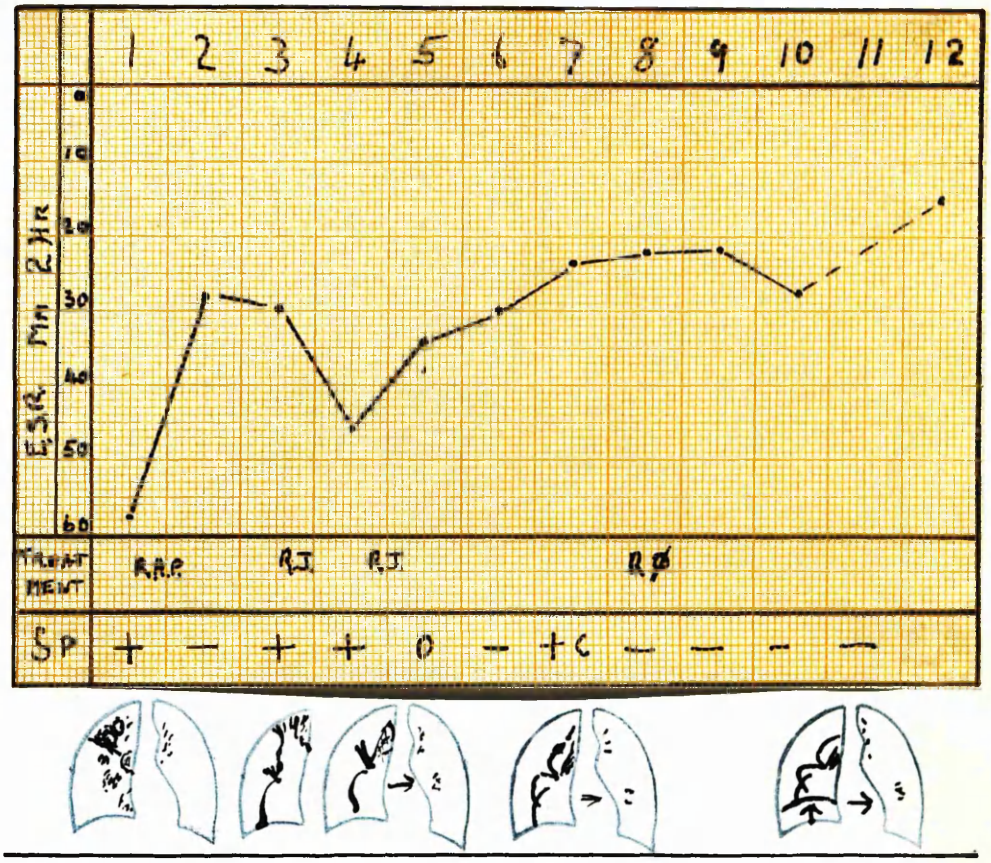
Admitted in fairly good general condition with diabetes melitus of 11 years duration which temporarily was out of control, but was controlled again with some difficulty by insulin and diet. He had a history of cough, sputum, huskiness commencing 6 months before admission, followed by haemoptysis and chest pain. The sputum was positive for tubercle bacilli two months before admission.

He improved rapidly after the induction of a right artificial pneumothorax and the cauterisation of adhesions in two sessions, which left him with the lung free except for an area on the upper mediastinum. The increase in E.S.R. after extensive cauteries is commonly seen. In this case the burnt area on the chest wall measured approximately $4\frac{1}{2}$" x $4\frac{1}{2}$"

Phrenic evulsion was performed to relax the tension on the mediastinal adhesion.

It is noteworthy that this diabetic who required 40 units of insulin daily tolerated an extensive cautery with the minimum of reaction.

CASE 10.


1 2 3 4 5 6 7 8 9 10 11 12
E.S.R. Mm 2 Hr
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60
TREAT MENT
R.R.P.
R.J.
R.J.
R.Ø
Sp
+ — + + 0 — +c — — — —

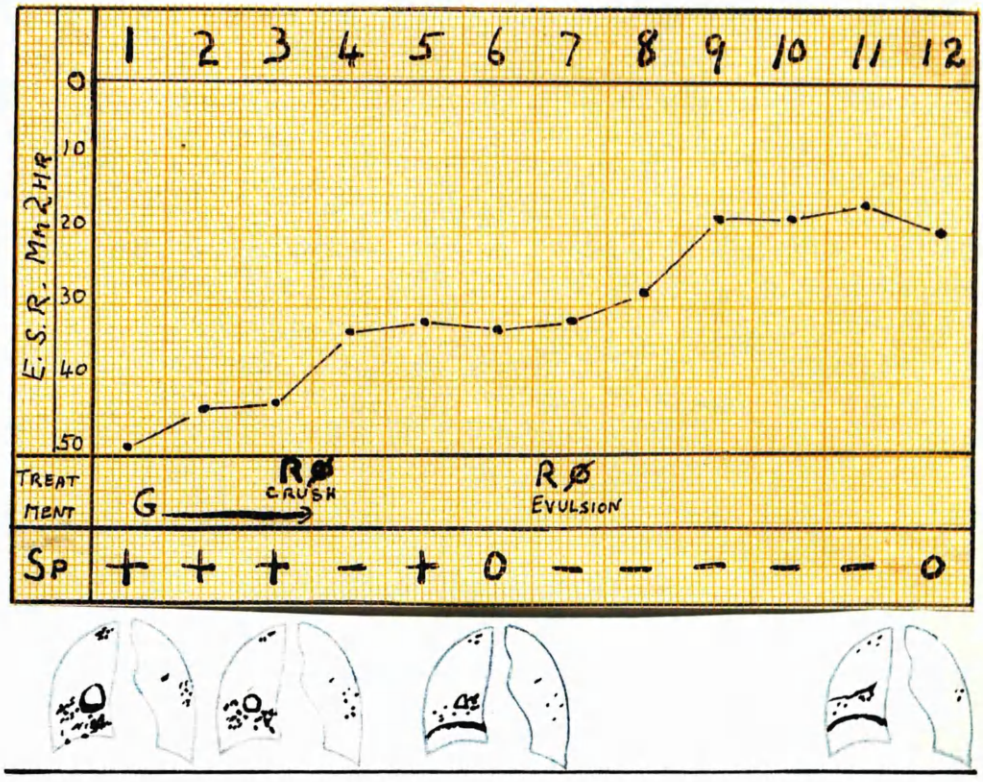
PHRENIC CRUSH AND EVULSION.

Case 11 (M.E.M.)

Admitted in rather poor general condition with cough, sputum, malaise and loss of weight of 6 months duration and more recent huskiness, chest pain and dyspnoea. The skiagram showed heavy tuberculous infiltration of the right lower lobe with a large cavity with fluid level. There were small opacities at the right apex and the left mid zone. Attempts to induce a right A.P. failed, and intravenous gold treatment commenced. The right phrenic nerve was crushed at the third month, when there was already some radiological improvement, with reduction in the size of the cavity. Improvement was progressive, and as the rise of diaphragm was influencing the diseased area the right phrenic nerve was evulsed at the 7th month. She was discharged symptomless at the 12th month, though there were still physical signs suggestive of cavitation in the right "dorsal lobe".

The thoracic surgeon did not consider her suitable for thoracoplasty.

CASE II.


1 2 3 4 5 6 7 8 9 10 11 12
E.S.R. Mm 2 HR
0
10
20
30
40
50
TREAT MENT
G
RØ CRUSH
RØ EVULSION
SP
+ + + − + 0 − − − − − 0

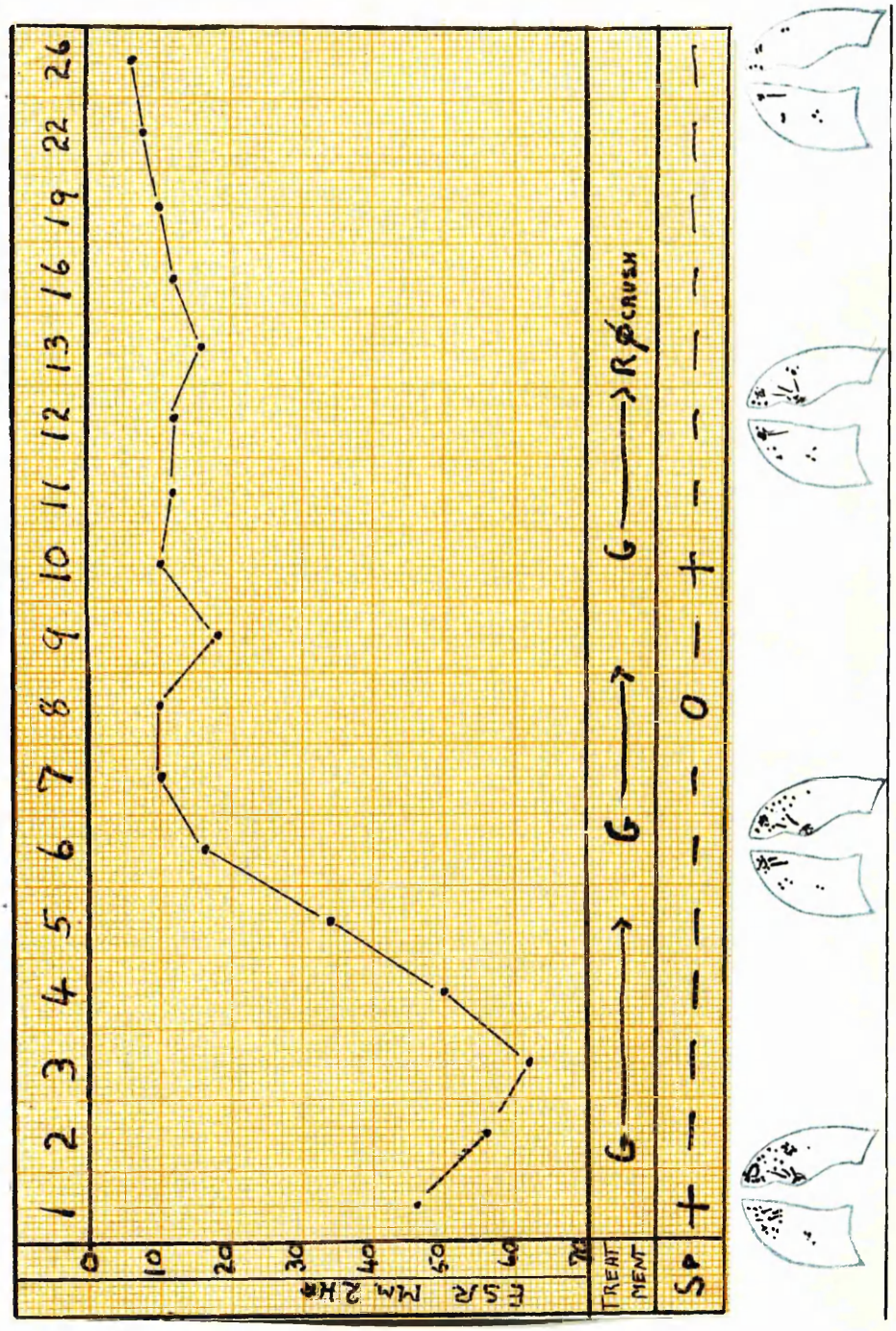
SANATORIUM ROUTINE AND GOLD TREATMENT.

Case 12 (J.W.R.)

Admitted in fair general condition with a history of left sided pleurisy with effusion 8 years ago, and recent cough, sputum, malaise and loss of weight. The skiagram showed bilateral lesions mainly productive in type, with cavitation at the left apex. Attempts to induce a left artificial pneumothorax failed. He was kept in bed for three months, intravenous crisalbine injections commencing during the 2nd month. Thereafter his progress through the sanatorium grades of excersise was rapid, and at 6 months he was up all day, walking for an hour and doing three hours moderate work. There was progressive radiological clearing though a cavity became visible in the right apex.

It is of interest, though possibly not significant that the only positive sputum specimen after the 1st month followed a slight rise in E.S.R. although the physical signs and symptoms were unchanged.

CASE 12.


1 2 3 4 5 6 7 8 9 10 11 12 13 16 19 22 26
0 10 20 30 40 50 60 70
FT SR MM 2 HR
TREAT MENT
G
G
G
R Ø CRUSH
Sp + - - - - - - - 0 - - - - - - - + - - - - - - - -

TUBERCLE ENDOTOXOID

Case 13 (D.S.)

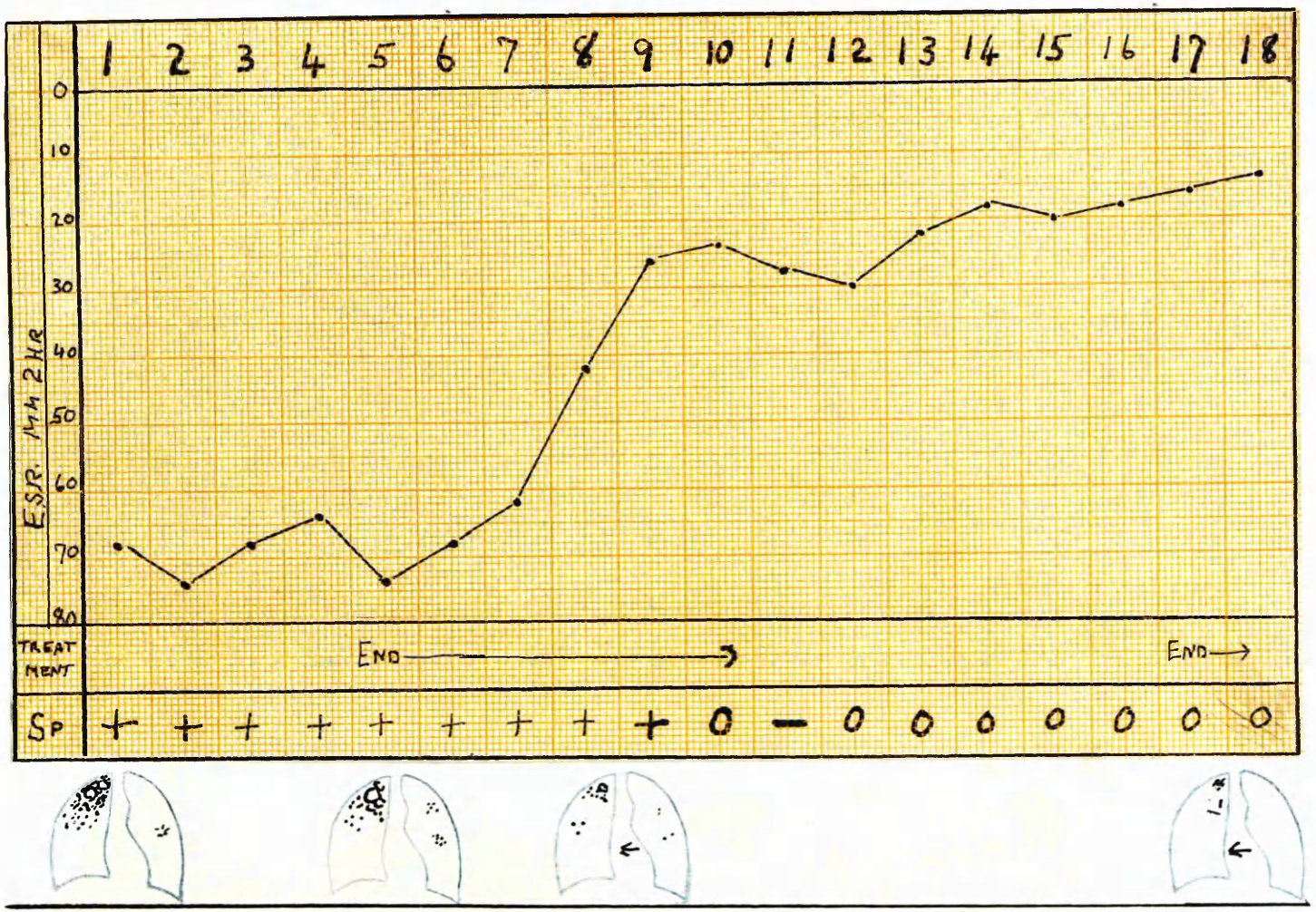
Admitted in fair general condition, but febrile, with cough, sputum and huskiness of 4 months duration, and more recent chest pain and loss of weight. The skiagram showed a massive exudative lesion with cavities, involving the whole right upper lobe, and a small area of infiltration in the left mid zone. Attempts to induce a right artificial pneumo-thorax failed. She was kept on strict bed rest for 5 months, by which time the temperature was settling. Then treatment by tubercle endotoxoid injections was commenced. This was well tolerated, and after three months she was allowed up and slowly progressed through the sanatorium grades of exercise. There was progressive radiological clearing until by the 18th month the skiagram showed a small apical cavity, diameter 1.5 c.m., in the centre of a localised shadow. She was symptomless, and well enough to commence training as a student nurse, and the lesion has remained stationary during 18 months of this work.

This case is of interest for two reasons:-

(i) It is the only case in a series of 20 in which striking improvement followed the administration of tubercle endotoxoid.

(ii) The satisfactory outcome in this case was unexpected in a girl of 16 not treated by collapse measures.

CASE 13.


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
0
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70
80
ESR. MM 2HR
TREAT MENT
END
END
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+ + + + + + + + + 0 — 0 0 0 0 0 0 0

PROGRESSIVE PULMONARY TUBERCULOSIS INFECTIVE HEPATITIS

Case 14 (W.H.S.)

Admitted in poor general condition. He had a history of cough and sputum for 20 years, and of illness for 1 year before admission. The skiagram showed diffuse tuberculous infliltration of both lungs with a small pleural effusion at the left base. Collapse therapy was contraindicated, but he improved at first despite an attack of infective hepatitis in the 3rd month which coincided with a sudden temporary improvement in the E.S.R. This slowing E.S.R. has been observed in other cases of infective hepatitis, but was not a constant feature of 12 of my own personal cases. Walton (1933) and others have observed a slowing of E.S.R. in some cases of liver damage.

Thereafter his condition deteriorated slowly, and there was evidence of haematogenous spread in the 9th month followed in the 10th month by symptoms of meningitis.

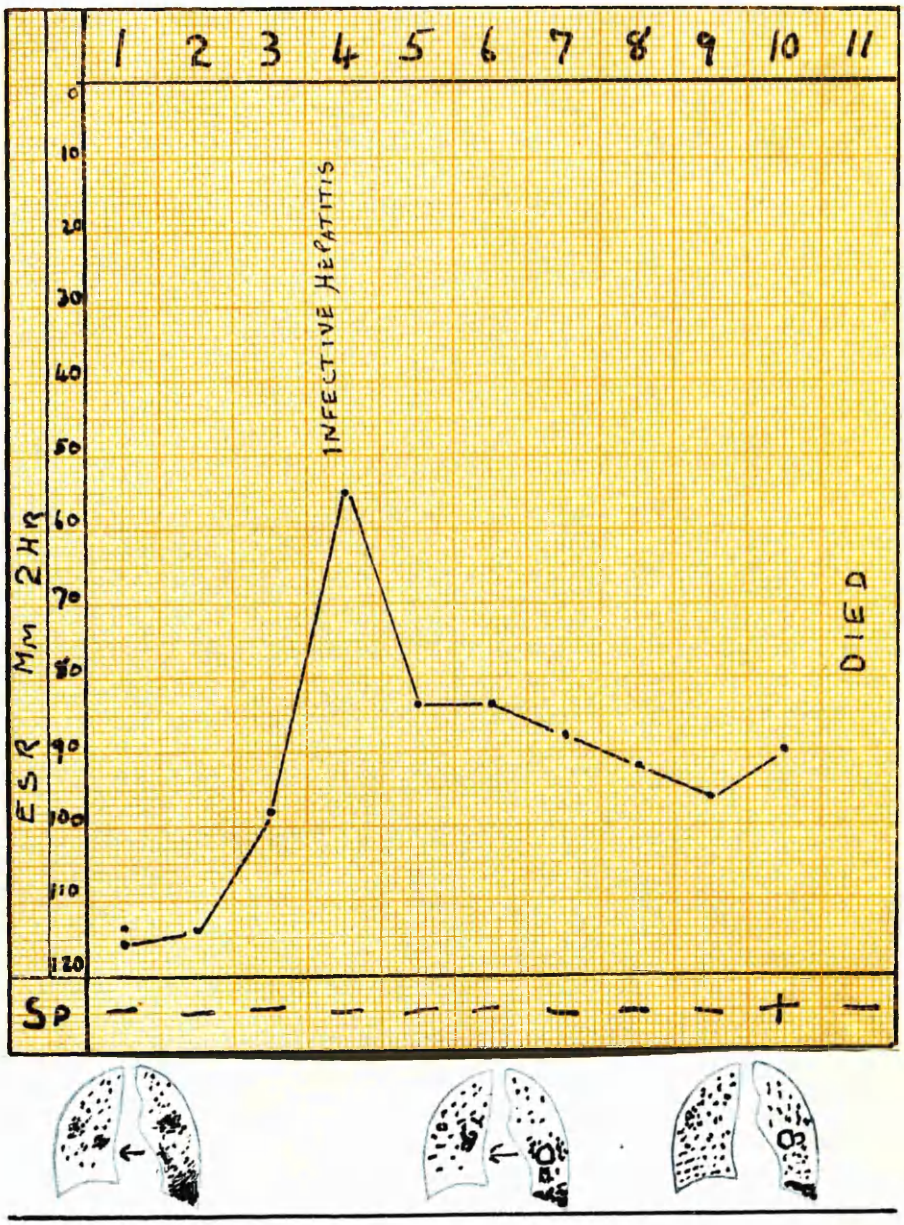
The E.S.R. persisting for any length of time at 80 mm/2nd hour or over indicates a very poor prognosis.

PHRENIC EVULSION FOLLOWED BY THORACOPLASTY

Case 15 (H.R.)

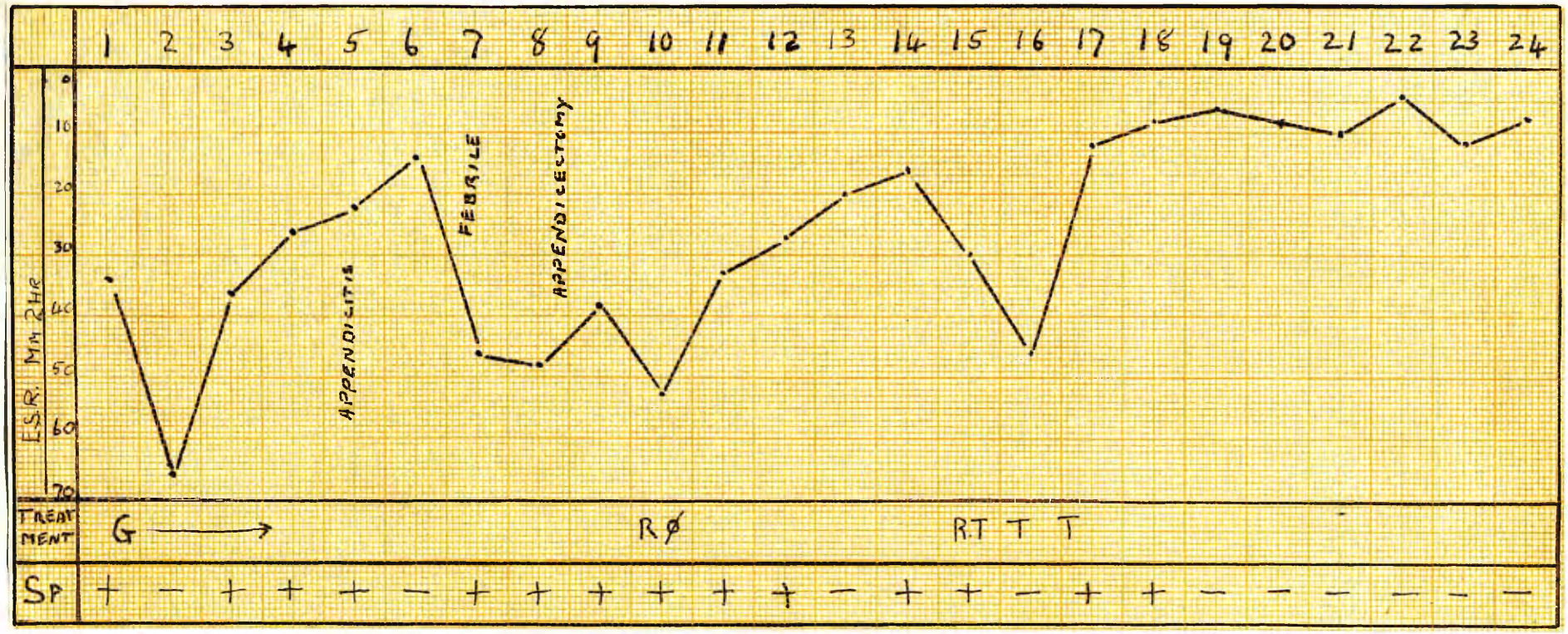
Admitted in good general condition with a history of cough, sputum, malaise and loss of weight for 2 months and recent chest pain at the left apex. The skiagram showed exudative mottling in the right upper and lower lobes, and in the left upper lobe, where there were possibly small cavities. A course of intravenous gold injections was given and was followed by some radiological improvement. At the 4th month a cavity had appeared in the right upper lobe. An A.P. induction was attempted, but failed. He had a slight attack of appendicitis at the 5th month, and slight jaundice which contra indicated further gold treatment. As the cavities in the right were larger he was seen by a thoracic surgeon who postponed decision regarding operative treatment as the general condition was not good and he was febrile. A further attack of appendicitis necessitated appendicectomy in the 8th month. As he was still unfit for major surgery at the 10th month the right phrenic nerve was evulsed. This was followed by a period of general improvement, including clearing of the left apical lesion. A ten rib paravertebral

CASE 14.


1 2 3 4 5 6 7 8 9 10 11
ESR MM 2HR
0 10 20 30 40 50 60 70 80 90 100 110 120
INFECTIVE HEPATITIS
DIED
SP
- - - - - - - - - + -

thoracoplasty was performed in three stages commencing at the 15th month. This was followed by a temporary deterioration in E.S.R. which one expects after blood loss and tissue damage. Thereafter he did well, though the lost weight was not fully regained, and at the 24th month he was transferred to a tuberculosis training colony where he has done useful work for over two years though the condition of the left lung has at times caused slight concern.

CASE 15.


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
E.S.R. MM 2HR
0 10 20 30 40 50 60 70
APPENDICITIS
FEBRILE
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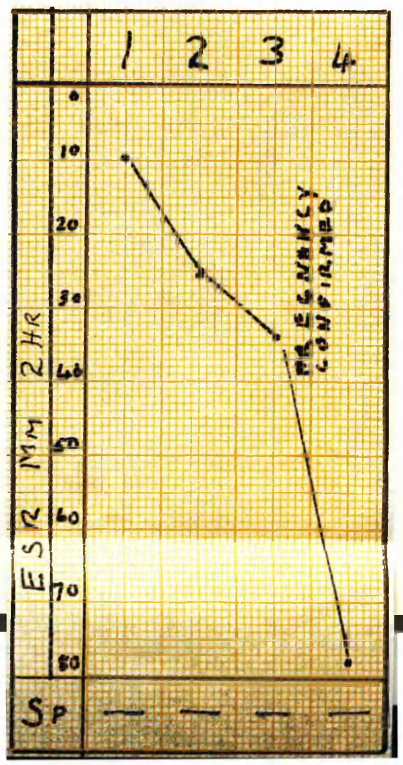
PREGNANCY

Case 16 (L.H.)

An unmarried girl of 20 was admitted in good condition, with 5 months history of slight cough, and sputum, dyspnoea, anorexia and malaise, followed by haemoptysis 3 months before admission. The skiagram showed a little suspicious shadowing outside the hila, and an enlarged hilar gland on the left.

Menstruation was said to be regular before admission, but from then onwards there amenorrhoea. The symptoms except dyspnoea, disappeared, and there was no change in the skiagram. The rising E.S.R. suggested the necessity for a fuller investigation, as it was considered unlikely that it was due to her tuberculosis. She was found to be $4\frac{1}{2}$ months pregnant.



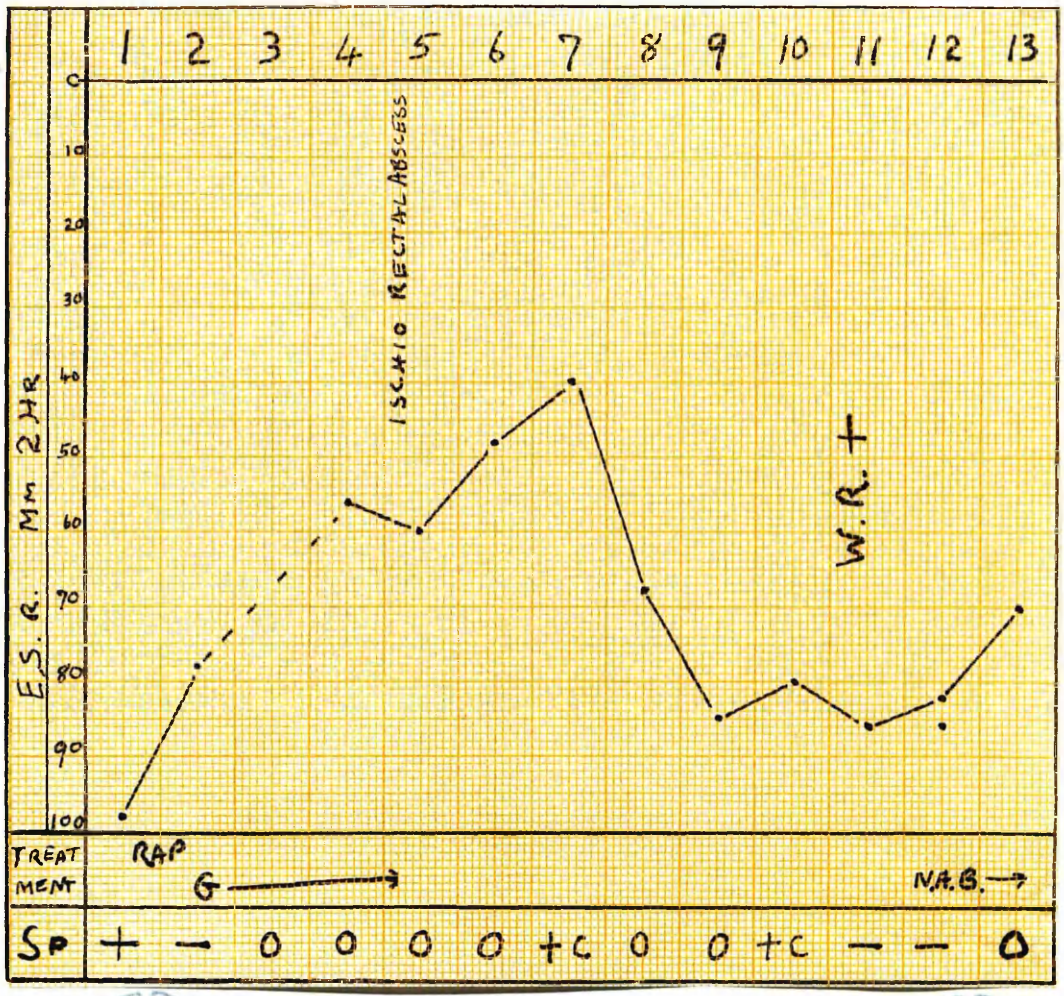
PULMONARY TUBERCULOSIS AND SYPHILIS.

Case 17 (P.L.)

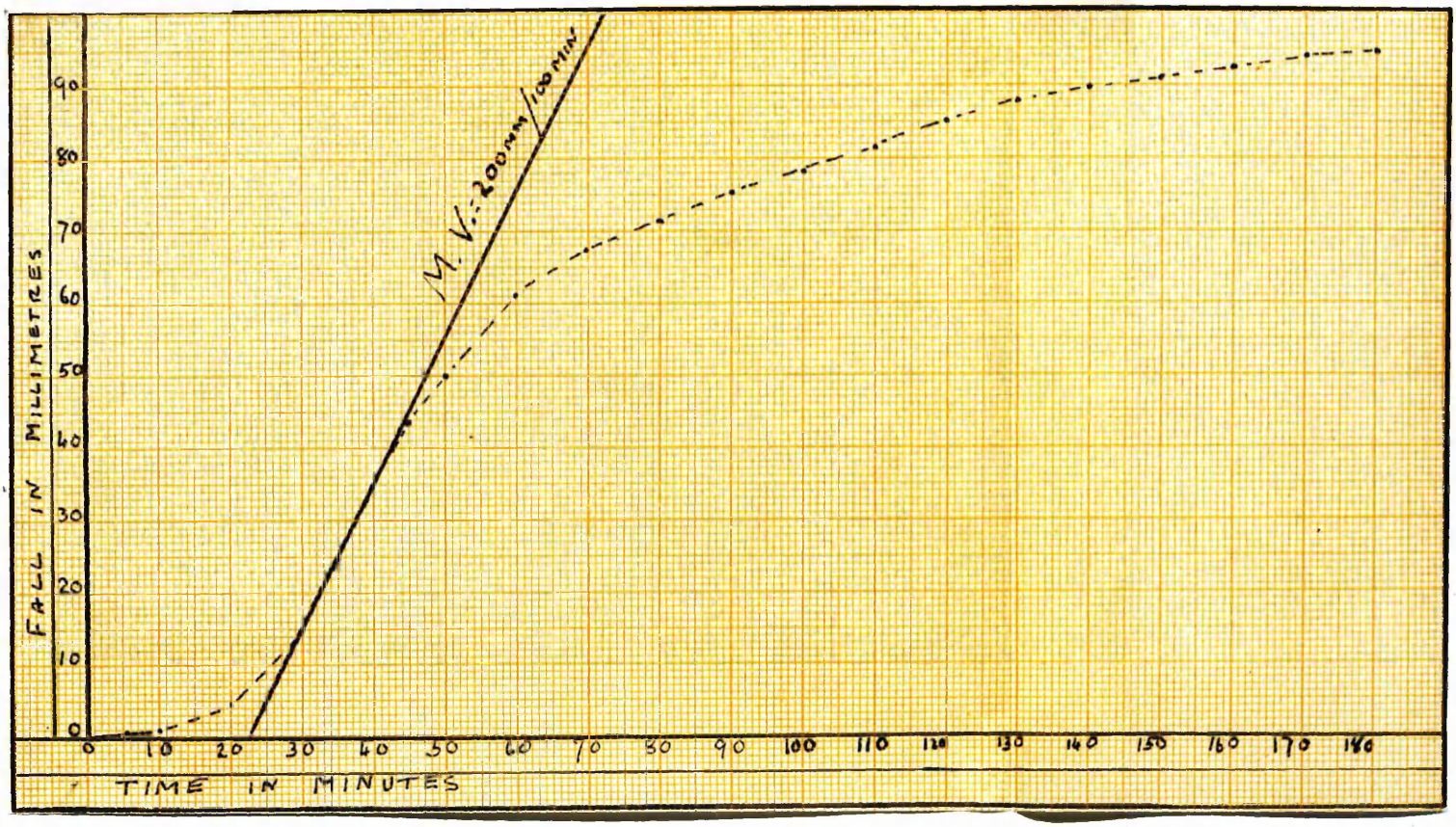
Admitted in fair general condition with four months history of chest pain, cough, sputum, anorexia, malaise and night sweats. The skiagram showed a dense contracting lesion with cavities in the upper third of the right lung, coarse mottling in the remainder of the right lung and discrete proliferative mottling in the left lung. The heart and mediastinum were drawn over to the right.

The right A.P. was only partially selective, and the adhesions could not be cauterised. But in spite of this and an ischio-rectal abscess which developed at the 5th month, he made reasonable progress. The deterioration in E.S.R. at the 8th month was at first blamed on the ischio-rectal abscess, for which a two stage operation was performed. But the stationary condition of his tuberculous lesions and the peculiar behaviour of his sedimenting blood (see chart) suggested that one of the other causes of rapid E.S.R. should be sought. The falling erythrocytes attained an unusual velocity for a very short time. It was almost impossible to take accurate readings. Then the fall continued at a much slower speed for another hour. His W.R. was strongly positive. No history of primary syphilis could be elicited.

CASE 17.


1 2 3 4 5 6 7 8 9 10 11 12 13
E.S.R. MM 2 HR
0 10 20 30 40 50 60 70 80 90 100
ISCHIO RECTAL ABSCESS
W.R. +
TREAT MENT
RAP
G
N.A.B.
SP + − 0 0 0 0 +C 0 0 +C − − 0

CASE 17. SEDIMENTATION GRAPH AT 9TH MONTH



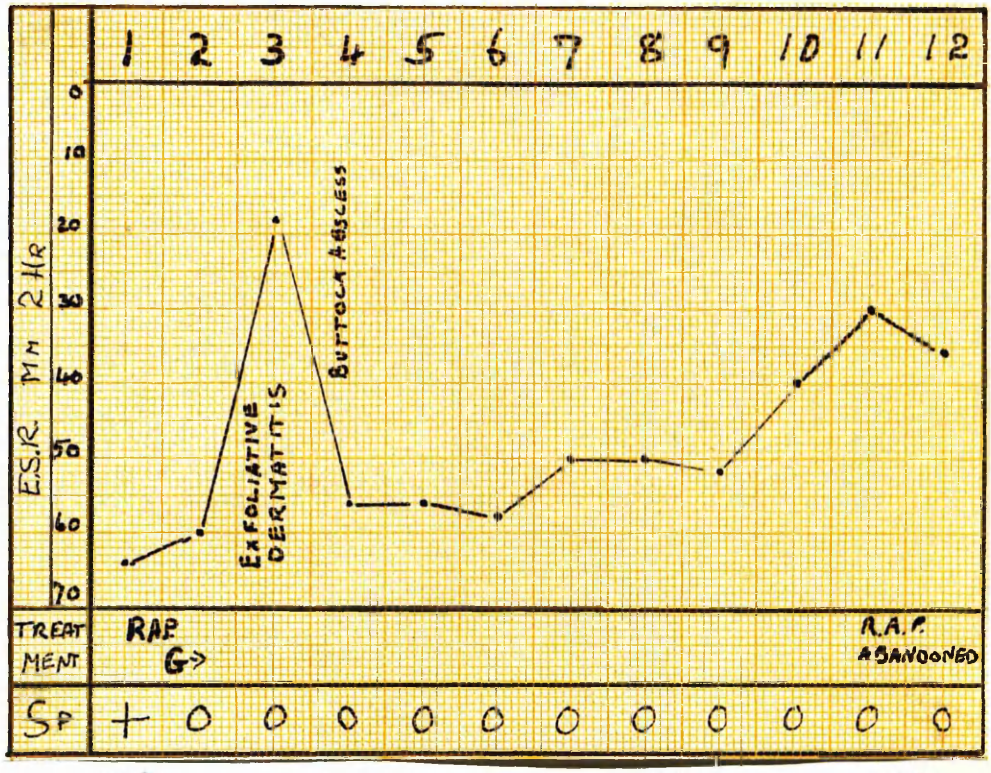
ANOMALOUS IMPROVEMENT IN E.S.R.

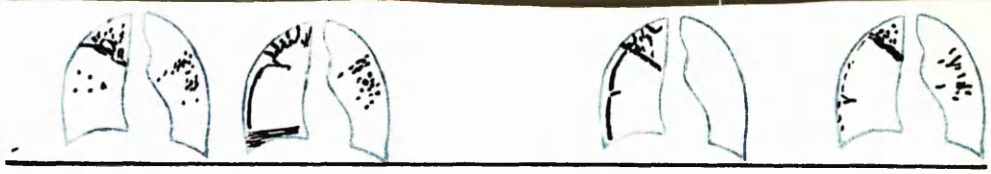
Case 18 (Mrs.A.)

Admitted in fairly good general condition, with a history of dry cough for a year, dyspnoea of long duration, and more recent huskiness, chest pain and scanty sputum. The skiagram showed a contracted right upper lobe with a cavity, some mottling in the right mid zone and heavy exudative mottling in the left mid zone.

A right artificial pneumo-thorax was induced and intravenous gold injections were commenced, but ceased after the second injection when a rash appeared which rapidly developed into a very severe exfoliative dermatitis with marked subcutaneous oedema. At this time the E.S.R. improved to a figure within normal limits - a change which obviously had no connection with the course of the tuberculous lesions. When the oedema subsided the E.S.R. returned to approximately its previous level. This suggests that the slowing might be due to haemo-concentration as a result of the oedema, but unfortunately this question was not investigated, and fortunately such cases are rare, and the opportunity for investigating a similar case has not occurred.

CASE 18.


1 2 3 4 5 6 7 8 9 10 11 12
ESR MM 2HR
0
10
20
30
40
50
60
70
EXFOLIATIVE DERMATITIS
BUTTOCK ABSCESS
TREAT MENT
RAP G>
R.A.P. ABANDONED
SP + O O O O O O O O O O O



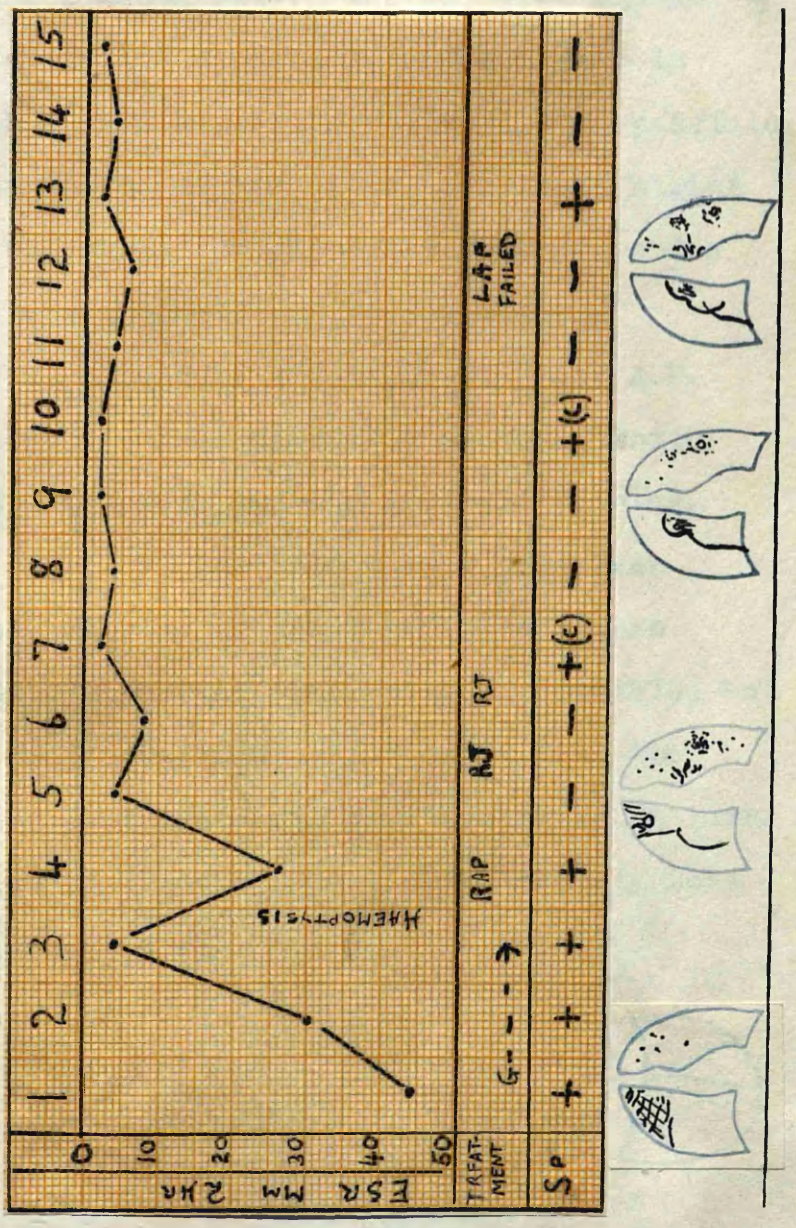
ANOMALOUS SLOW E.S.R.

Case 19 (A.L.)

Admitted in good general condition with a history of cough and sputum for three months. The skiagram showed an extensive lesion, mainly productive, of the right upper zone, which probably contained a cavity, and some scattered nodular mottling of the left lung field. After three months treatment by rest and gold injections, he had haemoptysis, and a Right A.P. was induced. The cavity in the right lung was then definitely seen. Adhesions in the A.P. were cauterised in two sessions during the 5th and 6th months. At this time a spread of the disease in the left mid zone was seen radiologically, though it was clinically silent, and the E.S.R. had reached normal limits. This new lesion showed cavitation at the 7th month and the cavity was still present at the 9th month, though the exudative lesion was small. Left A.P. was attempted at 12th month because of persistence of the small cavity and persistent positive sputum, but failed. He left the Sanatorium for economic reasons.

In this case the E.S.R. although it gave a good indication of the activity of the

disease on admission, failed to give any indication of the activity of the disease in the left lung, which progressed and cavitated in the presence of an E.S.R. within normal limits. In fact, at the 7th month the sedimentin index was 0.52, a figure which Day at one time claimed ruled out the possibility of pulmonary tuberculosis.



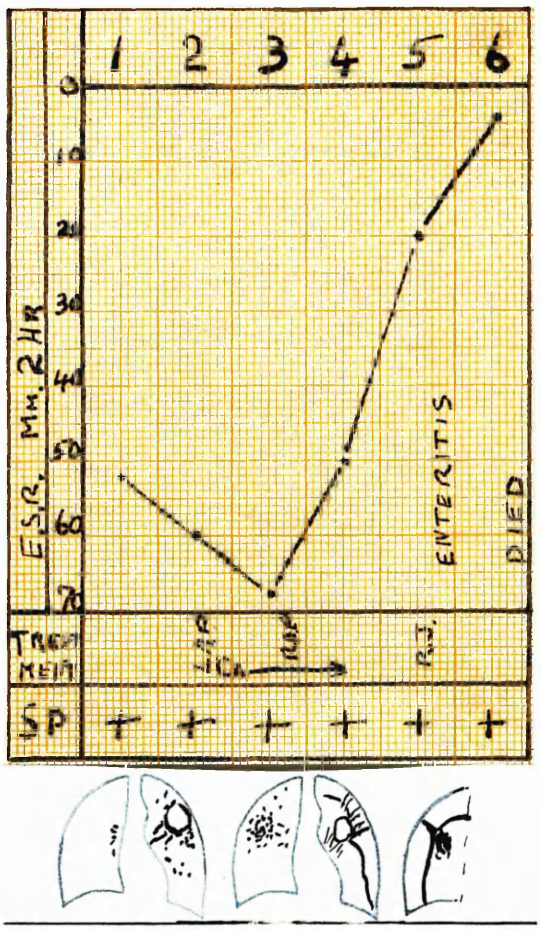
ANOMALOUS SLOW E.S.R.

Case 20 (D.B.)

Admitted in fair general condition, febrile, with a history of cough, sputum, and malaise for 1 month only. The skiagram showed a large cavity and much exudative mottling in the Left Lung and a perihilar spread with possible cavitation in the Right. After six weeks strict bed rest the condition was deteriorating, and a Left A.P. was induced, and as the disease continued to extend in the Right, a Right A.P. was induced as a last hope at 3 months. Toxic Enteritis developed, and she died at 6 months.

This is the only case I have seen of terminal slowing of the E.S.R., which has been reported by other observers. A possible, but unlikely explanation in this case is that the Enteritis caused haemoconcentration which in turn caused slowing of the E.S.R. Unfortunately this was not investigated.

CASE 20


1
2
3
4
5
6
0
10
20
30
40
50
60
70
E.S.R. MM. 2 HR
TREAT MENT
SP
+
+
+
+
+
+
ENTERITIS
DIED

PULMONARY FIBROSIS

Case 21(J.N.)

Admitted in fairly good general condition with a history of slight cough and spit since being gassed in 1918. There was a recent history of stained sputum and slight dyspnoea. The skiagram showed considerable contraction of the right hemithorax, with hard striated shadows in the lower half and increase of the lung markings. On the left the lung markings were increased and somewhat woolly. Tubercle bacilli were not found in the sputum. The E.S.R. was 2 mm/2nd hour.

Although this finding did not in itself rule out a diagnosis of pulmonary tuberculosis, it was of great help in arriving at the diagnosis of non tuberculous fibrosis of the lungs.

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